

**NATIONAL INSTITUTE FOR HEALTH AND CARE
EXCELLENCE**

Final appraisal document

**Ocrelizumab for treating primary progressive
multiple sclerosis**

1 Recommendations

- 1.1 Ocrelizumab is recommended, within its marketing authorisation, as an option for treating early primary progressive multiple sclerosis with imaging features characteristic of inflammatory activity in adults. It is recommended only if the company provides it according to the commercial arrangement (see section 2).

Why the committee made these recommendations

There are currently no disease-modifying treatments available for primary progressive multiple sclerosis. Results of 1 clinical trial show that ocrelizumab can slow the worsening of disability, although the size and duration of this effect are uncertain.

Given the unmet clinical need, the most plausible cost-effectiveness estimates for ocrelizumab at the agreed price compared with best supportive care alone are in the range that NICE considers an acceptable use of NHS resources. Because of this, ocrelizumab is recommended for treating early primary progressive multiple sclerosis with imaging features characteristic of inflammatory activity in adults.

2 Information about ocrelizumab

Marketing authorisation indication	Ocrelizumab (Ocrevus, Roche) has a marketing authorisation in the UK 'for the treatment of adult patients with early primary progressive multiple sclerosis (PPMS) in terms of disease duration and level of disability, and with imaging features characteristic of inflammatory activity'.
Dosage in the marketing authorisation	Ocrelizumab is administered by intravenous infusion. The first dose is administered as 2x300 mg infusions 2 weeks apart; subsequent doses are administered as a single 600 mg infusion every 6 months. There should be a minimum interval of 5 months between each dose.
Price	The list price for ocrelizumab is £4,790 per 300 mg vial (company submission). The company has a commercial arrangement (simple discount patient access scheme and commercial access agreement). This makes ocrelizumab available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

3 Committee discussion

The appraisal committee (section 6) considered evidence submitted by Roche and a review of this submission by the evidence review group (ERG). See the [committee papers](#) for full details of the evidence.

The condition and current care pathway

Primary progressive multiple sclerosis has a substantial effect on the lives of people with the condition and their families

3.1 Other than ocrelizumab, there are currently no disease-modifying treatments with a marketing authorisation for primary progressive multiple sclerosis. So, unlike for relapsing–remitting multiple sclerosis, clinicians can only offer interventions that manage symptoms. The patient experts explained that having a diagnosis of primary progressive multiple sclerosis often helps people understand the cause of their symptoms, but learning that there are no treatment options to slow the disease process can cause

anxiety. The experts further commented that people with the condition often have to reduce work commitments and may be unable to continue their usual daily activities. They highlighted the loss of confidence and depression that this causes, and that people feel the condition reduces what they are able to contribute to society. The committee noted the submissions it had received from patient and carer organisations, and comments received at consultation. These detailed how many people with primary progressive multiple sclerosis eventually need support and care from family members or friends, and that ocrelizumab has provided hope of slowing disability progression for people diagnosed with the condition. The committee concluded that primary progressive multiple sclerosis can substantially affect the lives of people with the condition and their families, and that disease-modifying treatments would be welcome.

Slowing disability progression and preserving upper limb function allow people to continue working, and to engage in everyday activities and self-care

3.2 A patient expert explained that, after starting treatment with ocrelizumab, his condition had improved. This had allowed him to keep working, particularly because of the treatment's effect on his upper limb function. In addition, patient experts and clinical experts explained that preserving upper limb function is important because it allows people to continue to care for themselves and reduces their reliance on others. The clinical experts noted that it is important to preserve upper limb function in all forms of multiple sclerosis. The committee noted that slowing disability progression allows people to stay in work and engage in everyday activities for longer than they may have done without treatment. It concluded that slowing disability progression and preserving upper limb function will allow people with primary progressive multiple sclerosis, as with other forms of multiple sclerosis, to continue working, engage in everyday activities and care for themselves for longer.

Diagnosing the condition is difficult and identifying who will benefit from ocrelizumab could increase demand for MRI scans

3.3 The clinical experts explained that diagnosing primary progressive multiple sclerosis is difficult because of the gradual, progressive nature of the condition, and the non-specific symptoms. In addition, it is hard to determine the time since onset of the condition because there is often no clear initial event. NICE must appraise drugs within the confines of the marketing authorisation determined by the regulators; the committee noted that the marketing authorisation limits treatment to early primary progressive multiple sclerosis with imaging features that are characteristic of inflammatory activity. The committee was aware that this needs either a single T1 MRI scan with a contrast agent (gadolinium) to identify acute inflammatory lesions, or at least 2 T2 MRI scans to identify new or enlarging lesions. A clinical expert explained that use of gadolinium is reducing because of concerns over longer-term safety, but that T2 scans could be used to identify inflammatory activity and to monitor change, and that they do not rely on an active lesion at the time of imaging. The company included the cost of an MRI scan, without contrast, per person having ocrelizumab in the economic model, and the cost of a further MRI scan, without contrast, for 70% of people (assuming that 30% of people with primary progressive multiple sclerosis would already have had a suitable MRI scan). A patient expert commented that repeated MRI scans are not currently done to monitor inflammatory activity because no disease-modifying treatments are available for primary progressive multiple sclerosis. The committee concluded that the use of ocrelizumab could result in increased demand for MRI scans.

Clinical effectiveness

It is appropriate to use data from the ‘MRI-active’ subgroup rather than from everyone in the ORATORIO trial

3.4 The company used the ORATORIO trial to provide evidence of the efficacy of ocrelizumab to treat primary progressive multiple sclerosis. ORATORIO was a double-blind placebo-controlled trial including 732 people from 29 countries. The committee noted that it did not enrol people aged over 55 years. A clinical expert commented that this is generally the case for trials in multiple sclerosis, and that the results could be considered generalisable to people in this age group. The committee further noted that the marketing authorisation for ocrelizumab was narrower than the inclusion criteria for the ORATORIO trial (that is, the entire or intention-to-treat population). The company explained that it had provided a post-hoc subgroup analysis of people in the ORATORIO trial with gadolinium-enhancing T1 lesions at screening or baseline, or with new T2 lesions between screening and baseline, to match the specification in the marketing authorisation for ‘imaging features characteristic of inflammatory activity’ (MRI-active subgroup). The committee noted that the trial was not powered for this group, so the real difference in treatment may have been missed. The clinical experts explained that the company’s method of identifying people with imaging features characteristic of inflammatory activity met accepted definitions. The committee concluded that it was appropriate to use data from the MRI-active subgroup from ORATORIO for decision making.

Defining early primary progressive multiple sclerosis is difficult in NHS practice

3.5 The marketing authorisation for ocrelizumab includes restricting treatment to primary progressive multiple sclerosis that is ‘early’ in terms of duration and level of disability. The company considered that everyone enrolled in

the ORATORIO trial met this definition; specifically, the trial included only people who, at screening, had:

- an expanded disability status scale (EDSS) score from 3.0 to 6.5 points
- a time since onset of symptoms of
 - less than 15 years if the EDSS score was more than 5.0 or
 - less than 10 years if the EDSS score was 5.0 or less.

The committee noted that the European Medicines Agency (EMA) had defined early primary progressive multiple sclerosis in the summary of product characteristics with reference to the main inclusion criteria of the ORATORIO trial. The clinical experts considered this to be too long to reflect ‘early’ disease, but also noted that there is no clear definition of early disease. The ERG commented that the clinical experts it had consulted suggested that they would define early disease as being within 5 years of symptom onset. The committee concluded that defining ‘early’ disease in NHS practice is difficult but that, for the purpose of this appraisal, early primary progressive multiple sclerosis is as defined by the EMA for the marketing authorisation.

It is not appropriate to limit estimates of clinical and cost effectiveness, and this guidance to people aged 50 years or under

3.6 The company provided clinical data from a subgroup of the MRI-active subgroup limited to people aged 50 years or under (that is, younger than the inclusion criteria of the trial), and modelled the cost effectiveness of ocrelizumab for this subgroup. The committee noted that the marketing authorisation does not specify an age threshold for treatment. It concluded that, in the absence of a clear biological rationale to exclude data from patients aged 50 to 55 years, it was not appropriate to define an age limit in this guidance.

Confirmed disability progression at 24 weeks is preferable to that at 12 weeks

3.7 The primary endpoint in the ORATORIO trial was time to disability progression confirmed after 12 weeks (‘confirmed disability progression’,

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CDP-12). Time to disability progression confirmed after 24 weeks (CDP-24) was a secondary endpoint. In the MRI-active subgroup, the treatment effect was slightly larger for CDP-12 (hazard ratio 0.68; 95% confidence interval 0.46 to 0.99) than for CDP-24 (hazard ratio 0.71; 95% confidence interval 0.47 to 1.06). The clinical experts commented that there is no consensus on what a 'clinically significant' effect is because there is no precedent for treating primary progressive multiple sclerosis. The committee noted that, in previous appraisals for relapsing–remitting multiple sclerosis, disability confirmed at 24 weeks (6 months) had been preferred because of higher specificity than disability confirmed at 12 weeks (3 months). The committee considered whether there were reasons why this should differ for primary progressive multiple sclerosis. A clinical expert commented that confirming disability after a longer period would be more reliable than after a shorter period in primary progressive multiple sclerosis, as it is in relapsing–remitting multiple sclerosis. The committee concluded that it preferred analyses using CDP after 24 weeks to after 12 weeks.

The treatment effect size estimated from the double-blind ORATORIO trial is preferable to using data from the open-label extension study

- 3.8 In response to consultation, the company provided estimates of treatment effectiveness that included data from an ongoing open-label extension of the ORATORIO trial combined with data from the double-blind treatment period. During the open-label extension, patients were made aware of their treatment allocation and those who had had placebo were able to switch to ocrelizumab. To calculate the treatment effect including the open-label data, the company used the Rank Preserving Structural Failure Time model to adjust for treatment switching. These data are academic in confidence so cannot be reported here. This resulted in estimated treatment effects for CDP-12 and CDP-24 that were greater than the effects estimated using data from the double-blind treatment period only. The ERG commented that using unblinded data increased the risk of both

performance and detection bias and, acknowledging this, the committee questioned why these data had been used. The company explained that the data decreased uncertainty by providing longer follow up, which captured a 'lag time' to maximum treatment effect. The committee noted that, unlike results from the double-blind period alone, the treatment effect was larger for CDP-24 than for CDP-12 when the open-label extension data were incorporated. The committee was aware that, in other NICE appraisals, observational follow up provides information on objective measures, such as death. However, it noted that disability progression is a subjective outcome and, compared with a double-blind study, an open-label study increases the risk of misclassifying outcomes. The committee concluded that using data from the open-label extension increased uncertainty about the size of the treatment effect. It further concluded that it preferred to use analyses that incorporated data from only the double-blind period of the ORATORIO trial, so it did not need to consider the methods that the company used to adjust for crossover.

Cost effectiveness

It is appropriate to include costs, disutilities and a treatment effect associated with relapses in the economic model

3.9 The clinical experts explained that relapses occur in primary progressive multiple sclerosis but do not characterise the condition in the way that they do for relapsing–remitting multiple sclerosis. The company excluded costs, disutilities and a treatment effect associated with ocrelizumab for relapses in its base-case model. The committee concluded that it would have been appropriate for the company to include costs, disutilities and a treatment effect associated with relapses in its base-case analysis. It noted that the company had done this in its revised base-case analysis submitted at consultation.

Adverse events

Infections and progressive multifocal leukoencephalopathy (PML) are possible adverse events associated with ocrelizumab

3.10 The committee questioned why the company had not included adverse events related to infection in the model, given that a high proportion of people in both the treatment (70%) and placebo (68%) arms of the ORATORIO trial had experienced infections. The company explained that it had focussed on a specific infection (upper respiratory tract infection), which occurred with the largest difference in frequencies between the ocrelizumab and placebo arms. The company explained that it could assign specific costs and utility values to upper respiratory tract infections, but not to aggregated infections. The committee also questioned why the company had not included PML in its model, noting that this had been considered as relevant in the then ongoing appraisal of ocrelizumab for relapsing–remitting multiple sclerosis. The company commented that it had included PML as an adverse event in an updated model for the relapsing–remitting multiple sclerosis appraisal, but only because it can be attributed to previous disease-modifying treatments. The company excluded it from the model for primary progressive multiple sclerosis because there have not yet been any recorded cases of PML after treatment with ocrelizumab in people with this condition. The clinical experts commented that PML is related to the treatment rather than the condition, and it would be inconsistent to consider that PML could occur in 1 type of multiple sclerosis, but not another. The committee concluded that ORATORIO was far too small and short to identify the real risk of PML. The committee concluded that there may be a risk of PML after treatment with ocrelizumab and that, if so, the economic model should include this. At consultation, the company submitted a revised base-case analysis that included PML as an adverse event.

It is appropriate to use registry data to inform baseline transitions between EDSS states

3.11 To inform the progression of disability between EDSS states in the absence of treatment, the company chose not to use data from the placebo group of the ORATORIO trial but instead to use data from a disease registry (MSBase) in its model. The company explained that it had used registry data because they reflect a larger population over a longer follow-up period. It also explained that it had chosen not to use registries that have been used in previous relapsing–remitting multiple sclerosis appraisals, such as the London Ontario registry, because these included few people with primary progressive multiple sclerosis. The ERG highlighted that MSBase was not restricted to people with primary progressive multiple sclerosis who had MRI scans showing inflammatory activity. The company acknowledged that limited MRI data are available from the MSBase registry, and the clinical experts confirmed this. Moreover, the clinical experts commented that many patients represented in the MSBase registry come from Eastern Europe, where the definition of primary progressive multiple sclerosis may differ from the UK. However, at consultation, the company commented that 80% of patients represented in the MSBase dataset came from Canada, Spain, Italy, the Netherlands and Australia. The committee also noted that there were few data available to inform estimates of transition probabilities between all EDSS states from the ORATORIO trial. It therefore concluded that it was appropriate to use the MSBase registry to inform baseline transitions between EDSS states in the absence of treatment in the company’s model.

Waning of treatment efficacy

Treatment efficacy may wane over time with ocrelizumab, but the absolute rate of waning is uncertain

3.12 The company assumed in its original base case that the relative treatment effect of ocrelizumab did not wane over time (that is, it worked equally well early and late in the course of treatment). It assumed this because ocrelizumab generates few neutralising antibodies, and because there was a sustained treatment effect in an open-label extension of a trial in relapsing–remitting multiple sclerosis. The company also assumed that people would stop taking ocrelizumab if they no longer gained benefit from it. Therefore, the company considered that including all-cause stopping of treatment in the economic model (see section 3.13) would act as a proxy for any waning of treatment effect in its original base-case analysis. The ERG considered it implausible that there is no waning of treatment effect and applied a decline in treatment effect from year 5. The ERG did this because treatment effect fluctuated over the course of the ORATORIO trial, and there was no evidence to show a long-term sustained effect. At consultation, the company submitted data from the most recent data cut of an ongoing open-label extension to the ORATORIO trial, which provided almost 6.5 years of data. The company used these to support a revised base-case analysis, which assumed a treatment waning effect from 10 years. The ERG commented that data from the open-label extension were reasonable evidence to support the absence of a treatment waning effect beyond 5 years, and revised its base-case analysis to assume a decline in treatment efficacy from 7 years. The committee noted that, in an appraisal for ocrelizumab for relapsing–remitting multiple sclerosis, the committee considered that treatment efficacy likely wanes over time. The committee concluded that the company's original assumption of no waning of treatment effect was too optimistic but that, acknowledging the issues of the open-label extension (see section 3.8), the ERG's approach may still be too

pessimistic. It concluded that the true waning of treatment effect is likely to lie between the company's and ERG's updated approaches, and that exploring assumptions of treatment waning from between 7 years and 10 years is reasonable.

Stopping treatment

There is considerable uncertainty about how long people would take ocrelizumab

3.13 The company modelled stopping of treatment (because of adverse events or because it does not work) by fitting a Gompertz distribution to data from the whole population rather than the MRI-active subgroup in ORATORIO. However, the company stated that 'clinical opinion' considered the average treatment duration predicted by this model to be too high (about 7.0 years). It provided what it considered a more realistic scenario analysis with a higher and constant treatment withdrawal rate, which predicted an average treatment duration of about 4.5 years. The ERG also used a Gompertz model in its base case, and considered that the rate of stopping treatment would rise as the effect of ocrelizumab waned (after 5.0 years in its original base case and 7.0 years in its revised base case; see section 3.12), adding this to its base case. The company's revised base case assumed an increase in the rate of stopping treatment at 5.0 years, to match the ERG's original base case. The ERG commented that this did not match its approach because it preferred to link treatment waning (by applying a reduced treatment effect) and an increased rate of stopping treatment. The committee considered that this approach may be too conservative because people remaining on the drug would be expected to show a good response, and would potentially not experience a reduced treatment effect. It concluded that there is considerable uncertainty about how long people would take ocrelizumab, but that the ERG's base case is likely to have overestimated the rate of stopping treatment.

There is considerable uncertainty about an appropriate stopping rule for disease-modifying therapies for primary progressive multiple sclerosis

3.14 Both the company and ERG assumed in their original base cases that people whose disease progressed to EDSS state 8.0 would stop ocrelizumab. The clinical experts commented that this was later than when people stop disease-modifying treatments in relapsing–remitting multiple sclerosis, which is when a person’s condition reaches and stays at EDSS state 7.0 for more than 6 months. Both the company and ERG assumed that treatment would stop when a person’s condition reached EDSS state 7.0 in their revised base cases. The clinical experts commented that an argument can be made for continuing treatment to EDSS state 8.0 because preserving upper limb function is particularly important once people are unable to walk. This was supported by comments from a patient group received during consultation. However, the committee and experts considered that this argument would apply equally to people with relapsing–remitting multiple sclerosis. The clinical experts noted that the ORATORIO trial enrolled people with multiple sclerosis with an EDSS only up to state 6.5, so there is no evidence for efficacy when starting treatment beyond this state, and that the ORATORIO trial did not have a stopping rule. The committee discussed the need for better disease models in multiple sclerosis. It concluded that, although there is considerable uncertainty, it had not been presented with any evidence to support a stopping rule that differed by type of multiple sclerosis.

Utility values

It is appropriate to use utility values from the ORATORIO study for EDSS states, supplemented by values from the literature

3.15 The company used utility values derived from the ORATORIO trial for most EDSS states in its base case. For EDSS states (0, 1, 8 and 9) for which ORATORIO offered no data, the company used utility values

specific to primary progressive multiple sclerosis from MS Trust survey data (Orme et al., 2007). The committee noted that the utility values from ORATORIO were higher than those from Orme et al. and another study in primary progressive multiple sclerosis (Hawton and Green, 2016). The company suggested that the utility values from ORATORIO were higher because people in the ORATORIO trial were younger (mean age 44 years) than in the other studies. The committee noted that the population for which NICE's recommendations apply include people aged over 55 years, who are not represented in ORATORIO. It also commented that a more recent publication than Orme et al. was available. At consultation, the company clarified, to the satisfaction of the committee, an issue of what appeared to be higher utility values for higher states of disability. The company also commented that people with inflammatory activity would be younger, and that few patients aged over 55 years would be eligible for ocrelizumab, based on data from the ORATORIO trial. The company believed that utility values from ORATORIO were a better match for the population within the marketing authorisation for ocrelizumab. The committee concluded that using different sources of utility data was acceptable when there were no trial data for EDSS states.

It is not appropriate to include additional utility decrements for upper limb dysfunction and fatigue

3.16 In addition to applying utility values for each EDSS state, in its original base-case model, the company also applied a utility decrement to each EDSS state for people with upper limb dysfunction and those with 'clinically meaningful fatigue'. The committee noted that upper limb function and fatigue were among 17 exploratory endpoints included in the protocol for ORATORIO. It questioned why the company had selected these outcomes to include in the model rather than the many other exploratory endpoints measured. The committee was aware of statistical principles for clinical trials from the regulators, which deem results only from planned analyses to be confirmatory. The company explained that

they did this because its analysis on data from ORATORIO showed that these factors affected health-related quality of life independent of EDSS state. The ERG disagreed with including additional utility decrements in the model, and did not include them in its own base case. It noted that ocrelizumab did not reduce fatigue (based on change in baseline score) in the MRI-active subgroup. It also noted that the company defined people as having clinically meaningful fatigue using cut-offs on the Modified Fatigue Impact Scale (MFIS). However, the ERG noted that cut-offs are not normally used with fatigue scores, and that most people entering the ORATORIO trial had fatigue based on the company's definition. The ERG also highlighted that previous appraisals for multiple sclerosis had not used specific utility decrements for symptoms associated with multiple sclerosis. The clinical experts commented that fatigue and upper limb function are equally important for people with relapsing–remitting multiple sclerosis. The committee noted that the company's approach would double-count disutilities incorporated within the EQ-5D because the MFIS and EQ-5D questionnaires overlap in some domains. At consultation, the company submitted a revised base case that excluded a utility decrement for fatigue, but still included a decrement for upper limb dysfunction. The ERG commented that the measure of upper limb function used in ORATORIO (changes in time to complete the 9-hole peg test) may not reflect changes in upper limb function that matter to people, such as reduced ability to wash, dress and feed themselves. The committee objected to using chosen selected exploratory endpoints in the modelling without considering the risk of false-positive findings. The committee still considered at its second meeting that including decrements for upper limb function, decreasing utilities as people progressed through EDSS states, and carer disutilities likely overestimated the effect of ocrelizumab on slowing disability progression. It therefore concluded that it was inappropriate to include utility decrements from upper limb dysfunction and fatigue in the economic model.

Cost-effectiveness estimates

Ocrelizumab is a cost-effective use of NHS resources

3.17 In a second revised base case, the company estimated the incremental cost-effectiveness ratio (ICER) for the MRI-active subgroup with an updated commercial arrangement. The company's model for this base case included the committee's preferred changes to the the company's original submission, and to its first revision. These were:

- including costs, disutilities and a treatment effect associated with relapses (see section 3.9)
- including the risk of PML (see section 3.10)
- using CDP-24 to estimate treatment effect (see section 3.7)
- removing a utility decrement for fatigue and for upper limb dysfunction (see section 3.16)
- using data from the double-blind period of the ORATORIO trial to estimate treatment effect (see section 3.8).

The company also provided 2 versions of its second revised base-case model, with treatment waning from either 7 or 10 years (see section 3.12). The ERG confirmed that the company's revised model reflected the committee's preferences. The ERG also re-ran the company's probabilistic analyses. The discount and the ICERs are confidential and the exact values cannot be reported here. The committee, in its third meeting, acknowledged that uncertainties remained about the true rate of treatment waning (see section 3.12) and how long people would continue to take ocrelizumab (see section 3.13). It again acknowledged that there is an unmet need for disease-modifying treatment for this condition (see section 3.1). The committee concluded that the most plausible ICER for ocrelizumab compared with best supportive care alone was within the range generally considered to reflect good value for treating conditions without any other treatment options. It further concluded that ocrelizumab, with the commercial arrangement, was cost effective for treating early

primary progressive multiple sclerosis with imaging features characteristic of inflammatory activity in adults.

Innovation

Ocrelizumab is an innovative treatment for primary progressive multiple sclerosis

3.18 The company stated that ocrelizumab is an innovative treatment because it is the only approved disease-modifying treatment for use in primary progressive multiple sclerosis. The committee noted that there is a considerable unmet need for treatment (see section 3.1) for this condition, so ocrelizumab reflects a 'step change' in treatment. The company stated that it believed its model captured all quality-adjusted life year (QALY) benefits. The committee agreed that ocrelizumab is a 'step change' in the treatment of primary progressive multiple sclerosis, and that it had not been presented with evidence of any additional benefits not captured in the QALY measurements.

Conclusion

Ocrelizumab is recommended for treating early primary progressive multiple sclerosis with imaging features characteristic of inflammatory activity in adults

3.19 Ocrelizumab slows disability progression compared with placebo, although the size and duration of the effect are uncertain. There is a large unmet need for treating primary progressive multiple sclerosis because no disease-modifying treatments are currently available (see section 3.1). The committee concluded that the ICERs generated by the economic model for treating early primary progressive multiple sclerosis with imaging features characteristic of inflammatory activity in adults represented a cost-effective use of NHS resources at the price reflected within the commercial arrangement.

4 Implementation

- 4.1 Section 7(6) of the [National Institute for Health and Care Excellence \(Constitution and Functions\) and the Health and Social Care Information Centre \(Functions\) Regulations 2013](#) requires clinical commissioning groups, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.
- 4.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final appraisal document.
- 4.3 When NICE recommends a treatment ‘as an option’, the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has primary progressive multiple sclerosis and the doctor responsible for their care thinks that ocrelizumab is the right treatment, it should be available for use, in line with NICE’s recommendations.

5 Review of guidance

- 5.1 The guidance on this technology will be considered for review 3 years after publication of the guidance. The guidance executive will decide whether the technology should be reviewed based on information gathered by NICE, and in consultation with consultees and commentators.

Amanda Adler
Chair, Technology Appraisal Committee B
May 2019

6 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.

Thomas Walker

Technical Lead

Rebecca Albrow

Technical Adviser

Donna Barnes

Project Manager

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