NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Final appraisal document

Ponesimod for treating relapsing-remitting multiple sclerosis

1 Recommendations

1.1 Ponesimod is recommended for treating relapsing-remitting multiple sclerosis with active disease defined by clinical or imaging features in adults, only if the company provides ponesimod according to the commercial arrangement.

1.2 This recommendation is not intended to affect treatment with ponesimod 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

Ponesimod is a disease-modifying treatment for multiple sclerosis. There are other disease-modifying treatments in routine clinical use.

Clinical trial evidence shows that people who have ponesimod have fewer relapses than people who have teriflunomide. Its effect on disability progression is not clear. Comparisons with other disease-modifying treatments are uncertain because of limitations in the clinical evidence.

The cost-effectiveness estimates are also uncertain, because of limitations in the clinical evidence and how long-term clinical benefit is predicted from short-term evidence. However, taking this uncertainty into account, the estimates are below

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what NICE normally considers an acceptable use of NHS resources. Therefore, ponesimod is recommended.

2 Information about ponesimod

Marketing authorisation indication

2.1 Ponesimod (Ponvory, Janssen) is indicated for 'the treatment of adult patients with relapsing forms of multiple sclerosis (RMS) with active disease defined by clinical or imaging features'.

Dosage in the marketing authorisation

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

Price

2.3 The list price for ponesimod is commercial in confidence so cannot be reported here. The company has a commercial arrangement (simple discount patient access scheme). This makes ponesimod 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 considered evidence submitted by Janssen, a review of the submission by the evidence review group (ERG), and responses from stakeholders. See the committee papers for full details of the evidence.

The condition

People would welcome new treatment options for relapsing multiple sclerosis

3.1 Multiple sclerosis is a chronic, lifelong disease with no cure, resulting in progressive, irreversible disability. It has many symptoms including pain, chronic fatigue, unsteady gait, muscle loss, speech problems,

incontinence, visual disturbance and cognitive impairment. Most people have the relapsing–remitting form of the disease, characterised by periods of new or worsened symptoms. The patient experts highlighted that the disease is complex and unpredictable and impacts all aspects of life and can affect carers too. The disease has a higher prevalence in women. Because it is typically diagnosed when people are of child-bearing age, the patient experts highlighted it is important to consider treatments that can be used during pregnancy. The company noted that although ponesimod is not indicated for pregnant women, its short half-life could be helpful for pregnancy planning compared with drugs with longer half-lives. The patient experts also highlighted that people generally prefer oral treatments and that ponesimod is an oral treatment. The committee concluded that despite many available treatments, people would welcome new treatment options for relapsing multiple sclerosis.

Treatment pathway, population and comparators

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

3.2 Ponesimod's marketing authorisation is for active disease defined by clinical or imaging features. The company explained that the ponesimod clinical trials included people with active disease defined as at least:

- 1 relapse within the last year or 2 relapses within the last 2 years, or
- at least 1 T1 gadolinium-enhancing lesion on brain MRI within the last 6 months.

The company positioned ponesimod as a first- or second-line treatment for active relapsing–remitting multiple sclerosis and considered ponesimod would not be used for secondary progressive multiple sclerosis. The company also provided evidence for the highly active subgroup as defined by the definition in the NHS treatment algorithm, which is people with an unchanged or increased relapse rate or ongoing severe relapses compared with the last year despite having previous

disease-modifying treatment. The clinical experts considered that the different forms of multiple sclerosis are part of a disease spectrum rather than having clearly defined aspects. However, they agreed with the company's positioning of ponesimod for these subgroups. The clinical experts agreed that ponesimod would be of value as a first-line treatment because:

- there are no oral treatments routinely available as first-line treatment for people who have only had 1 relapse in the last 2 years
- there are no treatments with ponesimod's mechanism of action routinely available for people who have only had 1 relapse in the last 2 years
- it has a shorter half-life than other treatments.

Having another first- and second-line treatment option would offer people more choice. The committee concluded that ponesimod was likely to be used as a first- or second-line treatment for people with active relapsing–remitting multiple sclerosis, and would not be used for secondary progressive multiple sclerosis.

All first-and second-line treatments used for relapsing–remitting multiple sclerosis are appropriate comparators

3.3 For people with active relapsing–remitting multiple sclerosis, the company submission compared ponesimod with beta interferons, dimethyl fumarate, glatiramer acetate, teriflunomide, ocrelizumab and peginterferon beta-1a. For people with highly active relapsing–remitting multiple sclerosis, the company submission compared ponesimod with alemtuzumab, cladribine, fingolimod and ocrelizumab. A comparison with ofatumumab and ozanimod for both groups was added at the clarification stage because they were being appraised at the time of the company submission, however ozanimod was not recommended. The clinical experts considered it unlikely that ponesimod would be the most effective treatment, but patients and clinicians would choose a treatment based on the risks and benefits. The committee noted that the most effective

treatments likely included monoclonal antibodies (alemtuzumab, ocrelizumab and ofatumumab), but that different treatment strategies are used depending on the person's preferences. The committee acknowledged that alemtuzumab is an induction therapy, and a safety review had restricted its use to highly active disease. But, because ponesimod is expected to be used for highly active disease, the committee concluded it should be considered as a relevant comparator for this subgroup. So, the committee concluded that all first- and second-line treatments for active relapsing–remitting multiple sclerosis were relevant comparators.

Clinical evidence

Ponesimod reduces relapses and fatigue-related symptoms, but its effects on disability progression are uncertain

3.4 The key clinical evidence for ponesimod came from 2 clinical trials in people with relapsing–remitting multiple sclerosis, and their long-term open-label extension studies:

- AC-058B201 (B201): a phase 2 placebo-controlled dose-finding trial and AC-058B202, an open-label uncontrolled extension trial for people who completed B201
- OPTIMUM: a phase 3 active-controlled (compared with teriflunomide) parallel trial with the licensed dose and OPTIMUM-LT, an open-label uncontrolled extension trial in people who completed OPTIMUM.

In OPTIMUM, the primary outcome was annualised relapse rate. Key secondary outcomes included change from baseline in fatigue-related symptoms, 3-month and 6-month confirmed disability accumulation and adverse events. In B201, the primary outcome was the cumulative number of new gadolinium-enhancing lesions from week 12 to 24. Key secondary outcomes included annualised relapse rate and the number of people with first confirmed relapsed disease from baseline to week 24. Both extension trials assessed long-term efficacy, safety and tolerability of

ponesimod. OPTIMUM showed a statistically significant difference in annualised relapse rate and change in fatigue-related symptoms for ponesimod compared with teriflunomide. However, there was no significant difference in 3-month and 6-month confirmed disability accumulation. The committee considered the differences seen in 3- and 6-month confirmed disability accumulation were uncertain and noted that this had a substantial effect on the cost-effectiveness results (see section 3.12).

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

3.5 The company used baseline characteristics from OPTIMUM in the economic model (see section 3.4). OPTIMUM included adults mostly from Europe. Inclusion criteria specified an Expanded Disability Status Scale (EDSS) score of between 0 and 5.5. People had been previously treated with interferon beta-1a, interferon beta-1b, glatiramer acetate, natalizumab or dimethyl fumarate, or had had no previous treatment. The trial excluded pregnant women or anyone with progressive multiple sclerosis. The clinical experts considered that the inclusion and exclusion criteria and the baseline characteristics in both trials were generalisable to people in the NHS with relapsing–remitting multiple sclerosis. The clinical experts added that people with milder disease (lower EDSS scores and fewer relapses) tend to be included in clinical trials. The committee concluded that the studies broadly aligned with other populations in clinical trials and were appropriate for decision making.

Fatigue is an important outcome measure, but is not included in the economic model

3.6 The company measured fatigue symptoms using the Fatigue Symptoms and Impacts Questionnaire: Relapsing Multiple Sclerosis (FSIQ-RMS). It considered that OPTIMUM was the first trial to use a validated disease-specific fatigue measure as a prespecified end point and to show that a disease-modifying treatment can stabilise fatigue symptoms. The patient

experts highlighted fatigue as an important element of quality of life and that some people would switch to a treatment that was shown to act on fatigue. The clinical experts suggested that ponesimod may reduce inflammation, which can reduce fatigue. The committee agreed that fatigue symptoms are an important element of the disease and that the FSIQ-RMS has potential to be an important disease outcome measure. However, fatigue was not explicitly included in the model and was instead captured through measuring health-related quality of life by EDSS score (see section 3.12). The committee also noted that because there was no evidence on fatigue symptoms from other clinical trials using the FSIQ-RMS, ponesimod could not be compared with drugs other than teriflunomide. The committee concluded that fatigue is an important outcome measure that was not explicitly modelled in the cost-effectiveness analysis. It was uncertain what effect fatigue would have on cost-effectiveness results without seeing data on how well the comparator treatments reduce fatigue.

Network meta-analysis

The results from the company's network meta-analyses are highly uncertain

3.7 To estimate ponesimod's relative effectiveness compared with all relevant comparators (see section 3.3), the company submitted network meta-analyses for the whole relapsing–remitting population and for the highly active subgroup. These were completed for 4 outcome measures: annualised relapse rate; 3- and 6-month confirmed disability accumulation; and treatment discontinuation. Because of differing inclusion criteria, the company included studies in which at least 80% of the trial population had relapsing–remitting multiple sclerosis according to OPTIMUM's criteria. The ERG considered the company's approach to the network meta-analyses to be generally appropriate. However, it highlighted the extreme heterogeneity of the trial designs, including large differences in how the placebo effect was reported across trials for all

outcomes. The ERG noted that the company made no attempt to address this heterogeneity (for example, by using meta-regression on baseline event rates), and considered it could bias the treatment effect. It considered that the outcomes of the studies included were short term and were unlikely to capture meaningful changes in disease. The relative treatment effects also had wide credible intervals, suggesting a highly uncertain treatment effect. For confirmed disability accumulation, which had a substantial effect on the cost-effectiveness results, the credible intervals of relative treatment effect of ponesimod crossed 1 for all treatments. This implied uncertainty that ponesimod was better or worse than any other treatment. To reduce heterogeneity in study design, at technical engagement the ERG suggested pooling interferons (see section 3.10). The clinical experts stated that the results of the network meta-analyses generally reflected which treatments are considered more effective in the NHS. The committee concluded that the network meta-analyses have major limitations and the results were highly uncertain.

It is appropriate to use 6-month confirmed disability accumulation in the network meta-analyses

3.8 The company used 6-month confirmed disability accumulation in its base case but considered the 3-month confirmed disability accumulation to be more robust to produce a network. The ERG considered the 6-month confirmed disability accumulation to be a more appropriate measure of progression and that this outweighed the additional data available for 3-month confirmed disability accumulation. The clinical experts also noted the long-established committee preference across recent technology appraisals for 6-month confirmed disability progression. The committee concluded that using outputs from the 6-month confirmed disability accumulation was appropriate.

The model provided an unexpected treatment effect for cladribine, based on 6-month confirmed disability accumulation

3.9 The committee noted that cladribine had a substantially higher treatment effect for 6-month confirmed disability accumulation than other treatments in the network meta-analysis for the highly active subgroup (see section 3.7). It noted that this estimate had wide credible intervals, indicating a high level of uncertainty. The committee noted that because 6-month confirmed disability accumulation had a substantial effect on the cost-effectiveness results (see section 3.12), this estimate also had a large impact on the cost-effectiveness estimate of cladribine. The clinical experts did not expect the substantially greater treatment effect for cladribine compared with other comparators in clinical practice, and anticipated cladribine's treatment effect to reflect the results from the full population analysis. In response to consultation, a stakeholder presented a published analysis that showed that cladribine has similar estimates of efficacy to higher efficacy monoclonal antibodies, when adjusting for baseline risk and considering different definitions of highly active disease. The committee considered that this could partially explain why cladribine seemed more effective in the network meta-analysis than in clinical practice, but also considered there could be some sampling error, indicated by the wide credible intervals.

It is appropriate to consider the results from the interferon studies in a hierarchical analysis, but the company's version was implemented incorrectly

3.10 The ERG noted substantial heterogeneity in the company's network meta-analyses, in part explained by varying treatment effects from interferon studies. To overcome this, the company provided an updated network analysis that considered all interferons as interchangeable, pooling them into a single node of the network. The ERG considered this appropriate and incorporated it into its base case. The clinical experts agreed that interferons could be presented as a class because they are considered similar in terms of efficacy and are treated as interchangeable in clinical

practice. The committee considered that it was potentially appropriate to consider the interferon trials using a class-based analysis. But it also requested a hierarchical class-based model, in which exchangeable effects are drawn from a class-level distribution rather than assuming a single, pooled treatment effect. The company provided this analysis in response to consultation and included it in its revised base case. The model excluded 2 trials that included interferon, ADVANCE and INCOMIN. The point estimates of the model reflected those from the previous models but it had substantially larger credible intervals for all comparator treatments. The committee considered that excluding the interferon trials did not meet the aim of requesting a hierarchical model and would have preferred the model to include them. The committee considered that the model must have been implemented incorrectly to create such wide credibility intervals, including for comparators that were not linked to an interferon. However, it noted that these changes to the network structure would mostly affect uncertainty parameters in the probabilistic analysis. The committee concluded that the hierarchical model would have been most appropriate if it had been implemented correctly. But it expected the results to lie between the pooled analysis and the company's original analysis with separate interferons and it considered both in its decision making.

All appropriate safety evidence for serious and rare adverse events with ponesimod has been considered

3.11 The company provided direct safety evidence from OPTIMUM and B201, including a long-term safety set which pooled evidence from everyone who had ponesimod during OPTIMUM and B201 and their long-term extension studies. The ERG noted that the safety data presented by the company was comparable to that of other disease-modifying treatments. But, it noted potential for an elevated risk of serious adverse events characteristic of the class of sphingosine 1-phosphate inhibitors. This would need confirming with long-term safety data from a large group. The clinical experts considered the adverse event profile would likely resemble

that of fingolimod, which has an acceptable safety profile. The ERG considered that adverse events had been appropriately included in the economic model. The committee considered that further data would be needed to fully establish ponesimod's safety profile but that all appropriate safety evidence had been incorporated in the economic model.

Economic model

The company's model aligns with previous models in the disease area but has limitations

3.12 The company's model structure was similar to model structures used in previous multiple sclerosis technology appraisals. It was a Markov transition model consisting of 20 health states (10 EDSS states for relapsing–remitting multiple sclerosis, 9 for secondary progressive multiple sclerosis, and death). The model used the British Columbia Multiple Sclerosis registry as a source of natural history data. Treatment effects for ponesimod and all comparators were from the company's network meta-analyses and were applied to adjust progression through each of the EDSS states using 6-month confirmed disability accumulation. Relapses were modelled independently, also using annualised relapse rate ratios from the network meta-analyses. The committee noted that many assumptions in the model had been accepted in previous technology appraisals in multiple sclerosis, including:

- modelling 1 line of treatment only with no treatment switching
- incorporating a treatment waning effect of 25% reduction in efficacy from years 2 to 5 and a 50% reduction in efficacy from year 6 onward (specific to technologies with a similar effectiveness profile, for example NICE technology appraisal guidance on peginterferon beta-1a and NICE technology appraisal guidance on dimethyl fumarate)
- relative risk of death being applied to each EDSS health state, taken from Pokorski (1997) which demonstrated risk of death because of multiple sclerosis was primarily dependent on disability

- incorporating patient utility values from published literature (Orme, 2007) rather than OPTIMUM.

The clinical experts considered that some of these modelling assumptions may not accurately represent the natural history of multiple sclerosis, or make use of the most up-to-date data. They added that differences in treatment efficacy are often driven by disease activity, the age of the person, the number of relapses and disability at baseline. The committee noted that previous appraisals had criticised the lack of treatment switching or sequencing and the fixed treatment waning effect as major limitations of similar models. It considered that these oversimplify what would happen in NHS clinical practice. However, it acknowledged that a model that can simulate treatment sequencing and variable treatment waning would be complex to construct and difficult to populate because of limited data. The committee considered that longer-term efficacy is difficult to establish and extrapolate from the short-term trials used in the network meta-analyses, the outputs of which have broad credible intervals. The committee concluded that the model structure and inputs broadly aligned with previous models in the disease area, but it had limitations.

The modelled output shows an unlikely number of people in high EDSS states

3.13 The committee noted that the modelled outputs from the company's model, including total quality-adjusted life year (QALY) gain, were inconsistent with those of other appraisals. The committee was unclear why this was the case if the inputs and structure were all broadly similar to those of previous appraisals. One of the main reasons for the differences between models was the conversion rate between relapsing–remitting multiple sclerosis and secondary progressive multiple sclerosis. The ERG noted that the London Ontario database was used to inform the conversion rates as reported in Mauskopf (2016), but these rates differed from those used in NICE's technology appraisal guidance on peginterferon. The ERG provided a scenario analysis that used the rates

used in the peginterferon appraisal and noticed that the cost-effectiveness results were sensitive to this assumption, though total QALYs remained low. The clinical experts commented that it would be plausible to assume that, in an average disease course, people would be in a relapsing–remitting multiple sclerosis state 50% of the time and in the secondary progressive multiple sclerosis state for the other 50%. But, they commented that some people will be in the relapsing–remitting state longer, particularly if their disease is treated early. The committee queried why the company analysis modelled that people would spend a greater amount of time in the secondary progressive multiple sclerosis state. Another important difference was the transition between EDSS states within secondary progressive multiple sclerosis, which were informed by the London Ontario database. The clinical experts stated that once the disease has progressed to secondary progressive multiple sclerosis, most people would remain in EDSS 6 or EDSS 7 states for a long period of time. The committee noted that a large proportion of people were in EDSS 8 and EDSS 9 for most of the model's time horizon and that both states had negative utility values. It considered that these results were unlikely and explained some of the differences in total QALY gain between appraisals. But, it was unclear which input was driving these transitions, because the transitions between EDSS states within secondary progressive multiple sclerosis had been used in previous appraisals. The committee was aware that the effect of this issue was uncertain because it was applied to all the modelled treatments. But, it did not see enough analysis to judge what would happen if more likely outputs were included. The committee concluded further sensitivity analysis was needed to explore unlikely numbers of people in high EDSS health states. In response to consultation, the company compared its model with the one in NICE's guidance on peginterferon. The ERG said that the outputs from both models were broadly in line. It added that if peginterferon inputs were used in the ponesimod model, both models produced similar secondary progressive multiple sclerosis time outputs with minimal difference between comparators. But the committee felt that

similarity with other appraisals did not necessarily indicate external validity. It also considered that this did not account for differences with other models or compared with clinical validation of the outputs. The committee concluded that this model, as with other multiple sclerosis models, is limited in its ability to accurately reflect the course of the condition, but considered that this model did show the relative benefit of ponesimod compared with comparator treatments. The committee concluded that the model should have more accurately portrayed the disease course of multiple sclerosis instead of showing an implausible number of people in high EDSS states. However, the committee concluded that the model demonstrated the relative benefit of ponesimod compared with other treatments sufficiently for decision making in this instance.

More appropriate mortality data may be available and should be used in future

3.14 The company initially used mortality data from Pokorski (1997) to model mortality within each EDSS health state, for both relapsing–remitting and secondary progressive multiple sclerosis. The company noted that this method has been used in several previous appraisals. The clinical experts considered that this mortality data was outdated and that managing acute infection and nursing has fundamentally reduced mortality with multiple sclerosis. They noted that new standardised mortality rates by EDSS state for people with multiple sclerosis had been recently published. This updated data showed higher risk of death in the EDSS states 8 and 9. When these rates were used to model mortality, it interacted with the implausibly high number of people in these states (see section 3.13) to produce overall survival that was substantially lower than that in the published data. The committee considered this implausible. The ERG considered that the new mortality model calculated mortality from few deaths and that there may be more appropriate sources of mortality data. It noted that this could be explored in a systematic review of mortality data in multiple sclerosis. For the purposes of decision making, the committee

considered both sources of mortality but noted their limitations. The committee concluded that in future appraisals in multiple sclerosis, it would like to see more appropriate sources of mortality data in a model with plausible distributions of people in EDSS states.

An economic model that accounts for treatment sequencing is needed to capture use of siponimod for secondary progressive multiple sclerosis

3.15 The ERG noted that siponimod has recently been approved for secondary progressive multiple sclerosis and the economic model did not allow for any treatment effect to be modelled after progression. The company obtained expert opinion that estimated 25% of people who develop secondary progressive multiple sclerosis would choose to have siponimod. However, the company and ERG base case only used the costs of siponimod use in the economic analysis. The clinical experts agreed that 25% of people with secondary progressive multiple sclerosis using siponimod seemed reasonable, but there was currently no data on uptake to base this on. They also noted that it was unlikely that siponimod would be offered to people whose disease progressed after they had ponesimod, because they both belong to the class of sphingosine 1-phosphate type 1 inhibitors. The clinical experts acknowledged there is no evidence for this and no studies exploring this assumption. The committee also questioned whether siponimod would be used by people with EDSS scores greater than 7, which was the health state that all treatments were stopped in the company assumptions. The clinical experts considered siponimod would not be offered to people with an EDSS greater than 7. This was confirmed by the NHS commissioning expert who noted that siponimod treatment would be stopped if a person is in EDSS 7 or greater for more than 6 months. The committee noted that this would be a large proportion of people in the modelled analysis because of the unlikely number of people in high EDSS states (see section 3.13). The committee concluded that the model did not allow for treatment sequencing that would reflect clinical practice and that including the costs but not the treatment effect of siponimod was not fully

consistent. However, it acknowledged that an economic model that can simulate treatment sequencing would be complex to construct and that minimal evidence for siponimod use would be available in current practice.

Cost-effectiveness estimates

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

3.16 NICE's guide to the methods of technology appraisal notes that judgements about the acceptability of a technology as an effective use of NHS resources will take into account the degree of certainty around the incremental cost-effectiveness ratios (ICERs). The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented. The committee noted the high level of uncertainty, specifically about the:

- results from the network meta-analyses (see sections 3.7 and 3.10)
- limitations of the model structure (see section 3.12)
- likeliness of the modelled output (see section 3.13)
- updated evidence on mortality (see section 3.14).

The committee considered both the population with active disease (at the point a person would receive their first treatment) and the subgroup with highly active disease (see section 3.2) separately. Taking into account the high level of uncertainty and potential benefits that were not captured in the model (see section 3.18), the cost-effectiveness estimates for ponesimod compared with other treatments for relapsing–remitting multiple sclerosis were below what NICE normally considers an acceptable use of NHS resources for the population with active disease. Because of confidential commercial arrangements for ponesimod and comparator treatments, the cost-effectiveness results cannot be reported here. For the subgroup with highly active disease, some cost-effectiveness results for ponesimod compared with cladribine and

alemtuzumab were above what NICE normally considers an acceptable use of NHS resources. However, the committee considered that the results for the comparison with cladribine may have been based on an unadjusted treatment effect (see section 3.9). It also considered that alemtuzumab offers different value because of its potential for good efficacy but with a high rate of adverse effects, and therefore patient choice was an important consideration. The committee concluded that overall, the cost-effectiveness results were acceptable and the most likely estimates were below what NICE considers an acceptable use of NHS resources.

Other factors

No equality issues have been identified

3.17 A patient expert questioned whether there is an equality issue about gender. The committee concluded that its recommendation applies equally to all genders, so this issue is not something that can be addressed in a technology appraisal. A patient expert submission highlighted concerns about disease-modifying treatment options during pregnancy. The committee noted that the summary of product characteristics states that ponesimod is contraindicated for pregnant women and women who can have children and are not using effective contraception. But it noted ponesimod's short half-life may be an important factor in choosing a treatment for people that will become pregnant. The committee also considered this could not be addressed in a technology appraisal.

Some benefits of ponesimod may not be captured in the economic analysis

3.18 The committee noted that there are no treatment options with ponesimod's mechanism of action available for all people with relapsing–remitting multiple sclerosis. It also noted that the effects of fatigue may not have been fully captured in the analysis (see section 3.6). It also noted other benefits such as the oral administration, short half-life and reduced

monitoring burden. The committee considered that these could lead to additional gains in health-related quality of life over those already included in the QALY calculations. The committee considered this in its discussions.

4 Implementation

4.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires 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 a relapsing form of multiple sclerosis and the doctor responsible for their care thinks that ponesimod 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. The guidance executive will decide whether the technology should be reviewed based on information gathered by NICE, and in consultation with consultees and commentators.

Sanjeev Patel
Chair, appraisal committee
December 2021

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.

Emily Leckenby and Elizabeth Bell
Technical leads

Adam Brooke
Technical adviser

Joanne Ekeledo and Daniel Davies
Project managers

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