Ponesimod for treating relapsing forms of multiple sclerosis

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

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

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

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?
Note that this document is not NICE's final guidance on this technology. The recommendations in section 1 may change after consultation.

After consultation:

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

For further details, see NICE's guide to the processes of technology appraisal.

The key dates for this appraisal are:

Closing date for comments: 25 October 2021

Second appraisal committee meeting: 4 November 2021

Details of membership of the appraisal committee are given in section 5
1 Recommendations

1.1 Ponesimod is not recommended, within its marketing authorisation, for treating relapsing forms of multiple sclerosis with active disease defined by clinical or imaging features in adults.

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

Treatments for relapsing multiple sclerosis include many disease-modifying treatments. These aim to reduce the number of relapses, slow the progression of disability, and maintain or improve quality of life.

Clinical trial evidence shows that ponesimod reduces the number of relapses compared with teriflunomide. However, ponesimod’s effect on disability progression is unclear. Comparisons with other disease-modifying treatments are limited by uncertainties in the clinical evidence.

The cost-effectiveness estimates are uncertain because of limitations in the clinical evidence and how long-term clinical benefit is predicted from short-term evidence. The estimates are above what NICE normally considers an acceptable use of NHS resources. Therefore, ponesimod is not 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, which would have applied if the technology had been recommended.

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 may be thinking about having children, 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 oral treatments are generally preferred 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 relapsing–remitting multiple sclerosis, stating it did not consider ponesimod would not be used for secondary progressive multiple sclerosis. The company also provided evidence for the highly active subgroup and agreed to define it as people whose disease progressed or remained unchanged within the last year despite having previous disease-modifying treatment. At technical engagement the company updated its positioning of ponesimod to exclude rapidly evolving severe disease, defined as people who had at least 2 relapses in the last year and at least 1 T1 gadolinium-enhancing lesion on baseline brain MRI. 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 drugs routinely available as first-line treatment for people who have only had 1 relapse in the last 2 years,
• there are no drugs 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 compared with 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.

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 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 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. The committee considered the differences seen in 3- and 6-month confirmed disability accumulation were uncertain.

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 between 0 and 5.5. People had been previously treated with interferon beta-1a, interferon beta-1b, glatiramer acetate, natalizumab or dimethyl fumarate, or 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 it 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 endpoint and show 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 drug 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, a key driver of the model, 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 company 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 it outweighs 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.

**Cladribine has the largest treatment effect based on 6-month confirmed disability accumulation, a key driver of the economic model**

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 is a key driver of the model (see section 3.12), this estimate also had a large impact on the cost-effectiveness estimate of cladribine. The clinical experts did not consider that cladribine shows a substantially greater treatment effect than other comparators in clinical practice, which is supported by results from the full population analysis. The committee considered that this anomalous result needs exploring further, particularly if there were any characteristics from the cladribine trials which could explain this.
It is potentially appropriate to consider the results from the interferon studies in a class-based analysis

3.10 The ERG noted heterogeneity in the company’s network meta-analyses because of varying treatment effects from interferon studies. To overcome this, the company adjusted the analysis to consider 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. However, the ERG considered a hierarchical analysis, assuming exchangeable effects drawn from a class-level distribution, would be more appropriate than pooling interferon treatments as though they had identical treatment effects. 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 noted that it had not been presented with goodness-of-fit statistics and inconsistency assessments for the network meta-analysis that pooled interferons. It also understood that the company had excluded several trials that compared interferons with each other from the pooled network, and noted that it would be helpful to include these. However, the committee understood that they would not contribute to estimates of treatment effect, but the measures of model fit would be comparable between approaches. The committee concluded that it was potentially appropriate to consider the interferon trials using a class-based analysis. However, it considered that a hierarchical class-based model may be more appropriate than assuming a single, pooled treatment effect. Further information on how well alternative approaches to pooling fit the data, and further sensitivity analysis showing the effect of different network meta-analysis assumptions on the cost-effectiveness estimates would be needed.

There is limited evidence for serious and rare adverse events of ponesimod

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 could be comparable with other disease-modifying treatments. But, it noted potential for an elevated risk of serious adverse events characteristic to 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 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. The model 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 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
• relative risk of death 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 critiqued 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 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 the modelled outputs, including total quality-adjusted life year (QALY) gain, from the company’s model were inconsistent with other appraisals. The committee was unclear why this was the case if the inputs and structure were all broadly similar to previous appraisals. One of the key drivers of 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 multiple sclerosis 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 key driver was the transitions between EDSS states within secondary progressive multiple sclerosis, which were informed by the London Ontario database. The clinical experts stated that once 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 make a judgement on 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.
Updated mortality data is available that isn’t included in the submission

3.14 The company 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 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 higher EDSS states 8 and 9. The committee was unclear how this would interact with the implausibly high number of people in high EDSS states (see section 3.13) to affect the cost-effectiveness results. The committee concluded that an updated analysis with the new mortality data would improve the accuracy of the model.

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

3.15 The company did not present any analysis that allowed for treatment switching or sequencing. The ERG noted that siponimod has recently been approved for secondary progressive multiple sclerosis and the economic model does 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 only 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 above 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 and including of interferons as a single class in the network (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 cost-effectiveness estimates for ponesimod compared with other treatments for relapsing–remitting multiple sclerosis were above what NICE normally considers an acceptable use of NHS resources. Because of confidential commercial arrangements for ponesimod and comparator treatments, the cost-effectiveness results cannot be reported here. The committee considered most of these limitations also applied to analyses for the highly active subgroup. A further issue about the treatment effect of cladribine in the network meta-analyses (see section 3.9) was unresolved.

Further analysis is needed to understand the impact of uncertainty in the economic model

3.17 The committee considered further analysis was needed to understand the impact of uncertainty on the economic analysis. This would include:

- further summary statistics and sensitivity analysis on the network meta-analyses, and particularly for interferons:
  - model fit statistics and analysis of inconsistency in the pooled analyses, including trials that compare different interferons with each other in the network, to make direct comparisons between different models possible (see 3.10)
  - a hierarchical class-based model for the interferons, assuming individual treatment effects within a class come from a distribution of effects with a class mean and between treatment variance within class
- analysis using updated mortality assumptions informed from new evidence
- further sensitivity analysis that produces more likely modelled outputs, including rate of secondary progressive multiple sclerosis progression and explanation of any inconsistencies of modelled outputs with previous appraisals.
Other factors

No equality issues have been identified

3.18 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.

All benefits of ponesimod are captured in the economic analysis

3.19 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 there were potential additional gains in health-related quality of life that could be attributed to these over those already included in the QALY calculations. The committee considered this in its discussions.

4 Proposed date for review of guidance

4.1 NICE proposes that the guidance on this technology is considered for review by the guidance executive 3 years after publication of the guidance. NICE welcomes comment on this proposed date. The guidance executive will decide whether the technology should be reviewed based
5 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 lead

Adam Brooke
Technical adviser

Joanne Ekeledo
Project manager