NICE National Institute for Health and Care Excellence

NICE guidance

Pitolisant hydrochloride for treating excessive daytime sleepiness caused by obstructive sleep apnoea

Technology appraisal guidance

Published: 9 March 2022
www.nice.org.uk/guidance/ta776

Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance are at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendations

1.1 Pitolisant hydrochloride is not recommended, within its marketing authorisation, to improve wakefulness and reduce excessive daytime sleepiness in adults with obstructive sleep apnoea whose sleepiness has not been satisfactorily treated by primary obstructive sleep apnoea therapy such as continuous positive airway pressure (CPAP), or who cannot tolerate it.

1.2 This recommendation is not intended to affect treatment with pitolisant hydrochloride 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

Excessive daytime sleepiness caused by obstructive sleep apnoea is usually treated with primary obstructive sleep apnoea therapy such as CPAP or mandibular advancement devices.

Clinical trial evidence suggests that pitolisant hydrochloride reduces excessive daytime sleepiness, with and without CPAP. But there is uncertainty about the evidence because of the way the trials were done. It is also uncertain how much pitolisant hydrochloride improves quality of life because of how it was measured in the trials.

Because of the uncertainty in the clinical evidence and economic model, the cost-effectiveness estimates are also uncertain. They are also likely to be higher than what NICE normally considers an acceptable use of NHS resources. So pitolisant hydrochloride is not recommended.

2 Information about pitolisant hydrochloride

Marketing authorisation indication

2.1 Pitolisant hydrochloride (Ozawade, Bioprojet Pharma) is indicated 'to improve wakefulness and reduce excessive daytime sleepiness (EDS) in adult patients with obstructive sleep apnoea (OSA) whose EDS has not been satisfactorily treated by, or who have not tolerated, OSA primary therapy, such as continuous positive airway pressure (CPAP)'.

Dosage in the marketing authorisation

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

Price

2.3 The list price of pitolisant hydrochloride is £138 for a 30-pack of 4.5-mg or 18-mg tablets (excluding VAT; company submission).

3 Committee discussion

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

The condition

Excessive daytime sleepiness caused by obstructive sleep apnoea affects quality of life

3.1 The patient expert explained that obstructive sleep apnoea can affect people's physical and mental wellbeing. Excessive daytime sleepiness affects daily life including education, employment, maintaining a social life and the ability to drive. Symptoms of sleep apnoea such as snoring can disrupt a partner's sleep, affecting their own quality of life. The patient expert said that a better understanding of the condition among GPs could improve consistency in arriving at a diagnosis sooner. The clinical experts noted that obstructive sleep apnoea can be associated with high blood pressure, heart disease and stroke. The committee concluded that excessive daytime sleepiness caused by obstructive sleep apnoea affects quality of life.

Pitolisant hydrochloride would typically be offered with CPAP, but some people cannot tolerate CPAP

3.2 The clinical experts advised that most people with excessive daytime sleepiness caused by obstructive sleep apnoea are referred to sleep clinics. Initial treatment includes lifestyle advice about weight loss. For people with mild symptomatic obstructive sleep apnoea, mandibular advancement devices are considered. For adults with moderate or severe obstructive sleep apnoea, NICE's technology appraisal guidance on continuous positive airway pressure (CPAP) recommends it for treating obstructive sleep apnoea. The patient expert explained that CPAP is usually well tolerated but some people may need to adjust to sleeping with a mask that is connected to a small machine. The clinical experts explained that some people cannot tolerate CPAP because they feel claustrophobic wearing a mask, which can be exacerbated by certain mental health issues. People with neurodegenerative conditions may also not tolerate

CPAP, and some people have anatomical variations that make CPAP unsuitable for them. The clinical and patient experts also explained that some people using CPAP will have residual excessive daytime sleepiness. They noted that pitolisant hydrochloride is a potential treatment option that would be welcome for improving excessive sleepiness, although it does not treat the underlying causes of obstructive sleep apnoea. The committee concluded that because pitolisant hydrochloride does not treat underlying airway obstruction, it would likely be used in addition to CPAP, but it acknowledged that some people cannot tolerate CPAP.

Mandibular advancement device availability varies across the country

3.3 The clinical experts explained that people who decline CPAP or cannot tolerate it may be offered a mandibular advancement device, which helps prevent the airway closing. They highlighted that this varies in practice because the devices are not available at every sleep clinic. About 20% of people who do not have CPAP might be offered a mandibular advancement device. However, because mandibular advancement devices are now recommended in NICE's guideline on obstructive sleep apnoea, they may be used more frequently. The company stated that mandibular advancement devices are generally used earlier in the treatment pathway than CPAP, so someone who declines CPAP is likely to have already been offered a mandibular advancement device. The committee concluded that because of the uncertainty around availability of mandibular advancement devices, it was appropriate to not consider them in this appraisal.

Pitolisant hydrochloride is likely to be prescribed in secondary care

3.4 The clinical experts highlighted that pitolisant hydrochloride would likely be prescribed in specialist sleep clinics (secondary care) because of the need to monitor adherence to CPAP. They highlighted that additional monitoring would be needed if pitolisant hydrochloride were recommended. They were uncertain if prescribing could move to primary care in the future. The committee concluded that pitolisant hydrochloride is likely to be prescribed in secondary care.

Clinical evidence

Pitolisant hydrochloride improves excessive daytime sleepiness, with and without CPAP

3.5 HAROSA 1 and HAROSA 2 were randomised trials of people having either pitolisant hydrochloride plus standard care (including lifestyle changes and CPAP optimisation for CPAP users) or placebo plus standard care, for a 12-week double-blind period. After 12 weeks, everyone in the trial was offered pitolisant hydrochloride for 40 weeks (the open-label phase). In HAROSA 1, people had been using nasal CPAP therapy for at least 3 months and had excessive daytime sleepiness before starting the trial. HAROSA 2 included only people who had not used CPAP and had excessive daytime sleepiness. The primary outcome of the trials was reduction in Epworth Sleepiness Scale (ESS) score. ESS scores of 10 or less indicate normal daytime sleepiness, and scores of 11 to 24 indicate excessive daytime sleepiness. The results showed a reduction in mean ESS scores from baseline to week 12 for the pitolisant hydrochloride group in both trials. In people who used CPAP, the mean ESS score reduced by 5.52 points in the pitolisant hydrochloride group. In people who had not used CPAP, the mean ESS score reduced by 6.30 points in the pitolisant hydrochloride group. In terms of quality of life, people in HAROSA 1 reported no statistically significant difference in EQ-5D or visual analogue scale score during the double-blind phase of the trial. However, there was an improvement in the pain and discomfort dimension of the EQ-5D in HAROSA 2. The clinical experts explained that an ESS reduction of 2 or more points could be considered clinically relevant, but noted that there is no clinical consensus about this because it will vary between individuals. The committee concluded that pitolisant hydrochloride improves excessive daytime sleepiness, with or without CPAP.

The HAROSA trials are broadly generalisable to NHS practice but may exclude some people who might be eligible for pitolisant hydrochloride

3.6 The HAROSA trials had a criterion that stated people with psychiatric illness could be excluded. The company clarified that people with depression were only excluded if the investigating clinician felt that it would make study participation challenging for them, rather than for any particular concern about comorbid conditions. A Beck Depression Inventory (13-item short form) score of less

than 16 was an inclusion criterion, meaning that people with mild (score 5 to 7) and moderate (score 8 to 15) depression were included in the HAROSA trials. The company stated that the trials included people with depression and anxiety. There were 18% of people in HAROSA 1 and 5% in HAROSA 2 who had a pre-existing psychiatric illness. The committee noted that the company's submission stated that about half of people with severe excessive daytime sleepiness have coexisting depression. The clinical experts estimated that about half of people referred to sleep clinics might have antidepressant therapy of some kind. The committee accepted that some people with depression were included in the trials, but the proportions were lower than might be expected in the NHS. This might affect the generalisability of the trial data. The effect of this on the clinical-effectiveness estimates was unknown. The committee concluded that the HAROSA trials were broadly generalisable for decision making, but may under-represent people with psychiatric illness.

Adherence to CPAP is unlikely to be affected by treatment with pitolisant hydrochloride

3.7 The patient expert explained that some people with excessive daytime sleepiness may prefer to manage their symptoms with medicine, rather than using CPAP. So they might use CPAP less often when taking pitolisant hydrochloride, which could lead to a reduction in the combined benefits of CPAP and pitolisant hydrochloride. The clinical experts said that most sleep clinics can remotely monitor CPAP use. Some people, such as heavy goods vehicle drivers, regularly have their CPAP use monitored remotely. The clinical experts stated that people having pitolisant hydrochloride alongside CPAP may have their use monitored more frequently than in current practice. The committee concluded that CPAP use is unlikely to be affected by treatment with pitolisant hydrochloride, because of regular monitoring. In response to consultation, the patient expert reiterated concerns that people having pitolisant hydrochloride in addition to CPAP may use their CPAP machine less often. The committee acknowledged concerns about reduced CPAP adherence, but concluded that it had not seen evidence to change its original conclusion that pitolisant hydrochloride use is unlikely to affect CPAP use.

A trial of pitolisant hydrochloride for narcolepsy had a follow-up period long enough to understand its side effects

3.8 The clinical experts had experience using pitolisant hydrochloride with people who have narcolepsy. They commented that they could rapidly see the benefits as well as the side effects of the treatment. The company provided data from HARMONY, a study of people taking pitolisant hydrochloride for narcolepsy for 1 year or more. The ERG cautioned that the effectiveness of pitolisant hydrochloride in HARMONY does not directly correlate to effectiveness in obstructive sleep apnoea because the cause of sleepiness is different. The committee concluded that the HARMONY follow-up period was long enough for decision making about the side effects of pitolisant hydrochloride.

The economic model

The company's new model is acceptable for decision making but has limitations

3.9 The company's original model was based on a model developed by McDaid et al. (2007) for NICE's technology appraisal guidance on CPAP for treating obstructive sleep apnoea. The model in that appraisal included a method of mapping ESS scores to EQ-5D utility values (from now, the McDaid approach). The ERG noted that pitolisant hydrochloride and CPAP treat different aspects of the condition, so following the CPAP model may not be the best approach for evaluating pitolisant hydrochloride. However, it stated that the relevant consequences of the comparisons could be adequately assessed using this model, although it may be more complicated than necessary. It corrected some aspects of the company's model, which had a small effect on the company's base-case incremental cost-effectiveness ratio (ICER). But the committee was interested in a model that considered people with a disease response and those without, separately, and explored placebo adjustments (see section 3.11). Restructuring the model in this way, and adjusting for a placebo effect, might reveal greater differences between the 2 groups. In response to consultation, the company submitted a new model similar to the one used in NICE's technology appraisal guidance on solriamfetol for treating excessive daytime sleepiness caused by obstructive sleep apnoea. The new model included a decision tree for the first 52 weeks of treatment followed by a Markov model with 3 health states: 'responder', 'non-responder' and 'death'. Movement

through the model was based on disease response. The company assumed that people who had standard care could be considered 'responders'. The model adjusted for the Hawthorne effect using a centring approach. The ERG agreed that the new model was consistent with the committee's comments from the first meeting about response status and adjustment for a placebo effect. However, it noted several limitations, including:

- no explanation of how baseline utility values were derived
- errors in the formulas used to map ESS scores to EQ-5D utility values using the McDaid approach, which resulted in overestimated values
- uncertainty around the response transition probabilities informed by stopping treatment
- it did not include probabilistic sensitivity analyses, so the probability that pitolisant hydrochloride is cost effective is unknown.

The committee questioned the company's approach of assigning utility values based on both response status and treatment group. It acknowledged the limitations of the new model but concluded that it was acceptable for decision making.

There is no direct evidence that pitolisant hydrochloride reduces cardiovascular events

3.10 The company's original model assumed that a reduction in ESS score was related to a reduction in cardiovascular disease risk (that is, people could move into the post-coronary heart disease state if they had an acute cardiovascular event and survived). The original modelling also assumed that pitolisant hydrochloride lowers the risk of cardiovascular events, which are more prevalent in people with excessive daytime sleepiness caused by obstructive sleep apnoea. The committee noted that the company did not explain the biological mechanism by which pitolisant hydrochloride may reduce cardiovascular events. The clinical experts explained that because of the lack of long-term clinical trials in obstructive sleep apnoea, they rely on markers for cardiovascular risk such as blood pressure. They stated that there is evidence that people using CPAP have reduced blood pressure along with their daytime sleepiness. But they noted that there was no direct evidence to validate this assumption in the economic model. The ERG agreed that it had not seen evidence that a reduction in ESS score with pitolisant hydrochloride would lead

to a reduction in cardiovascular events. It was unaware of any reasonable mechanism by which a wakefulness drug would reduce cardiovascular risk, rather than this being a result of treating the underlying cause of excessive sleepiness (obstructive sleep apnoea). The committee noted that the HAROSA trials showed no changes in people's blood pressure levels. In the absence of evidence of changes in cardiovascular markers, the committee agreed with the ERG. It concluded that there was no direct evidence of a clinical or biological mechanism by which pitolisant hydrochloride affects cardiovascular events. In response to consultation, the company provided a new model that did not include a potential effect of pitolisant hydrochloride on the risk of cardiovascular events (see section 3.9). The committee noted this was consistent with its conclusion at the first committee meeting.

Adjusting for the Hawthorne effect is the most appropriate approach to adjust for the placebo effect

3.11 The ESS score improved from baseline to week 12 in the placebo group in both HAROSA trials. The clinical experts suggested this could be because of potential observation bias from the Hawthorne effect (that is, people reported an improvement in ESS scores because they have more frequent contact with trial investigators than they would with clinicians in clinical practice). The committee noted the potential causes of such an effect and discussed ways to adjust for it. One way might be to remove the improvement in ESS scores observed in the placebo group from both the placebo and the pitolisant hydrochloride groups in the model (sometimes referred to as a centring approach). At its first meeting, the committee concluded that approaches to account for the placebo effect shown in the HAROSA trials should be explored to understand its effect on the cost-effectiveness results. In response to consultation, the company submitted a new model that adjusted for the placebo effect using a centring approach, under the assumption that placebo group improvements were a result of the Hawthorne effect. The ERG provided additional scenarios that assumed:

- a true placebo effect (adjusted for by removing the treatment effect for placebo for comparator group, but keeping it in the pitolisant group)
- a regression to the mean effect (no adjustment based on the assumption that the trial may have captured extreme ESS scores that would trend towards the mean over time) or

- an equal contribution from the 3 proposed effects.

The ERG noted that the regression to the mean model would only be appropriate if it was evident that people's ESS scores fluctuated over time. The clinical experts explained that there is limited long-term ESS score data for people who are having treatment for excessive daytime sleepiness. The experts added that in clinical practice, they observe some fluctuation in people's ESS scores. The committee noted that it had not seen evidence of how much people's ESS scores fluctuated over time. It concluded that adjusting for the Hawthorne effect by removing the treatment effect for placebo from the comparator and pitolisant hydrochloride groups was the most appropriate approach to adjust for the placebo effect.

The EQ-5D utility values from both the trials and the McDaid mapping approach are relevant for consideration

3.12 The company stated that the EQ-5D questionnaires may not adequately capture quality-of-life benefits in people with obstructive sleep apnoea. It explained that because EQ-5D is a generic instrument, it is not designed to specifically measure changes in quality of life for people with excessive daytime sleepiness caused by obstructive sleep apnoea. It also noted that the EQ-5D does not have a sleep domain, which means improvements in sleep or daytime wakefulness are unlikely to be captured. So the company's submission mapped ESS scores from the trials to the EQ-5D (the McDaid approach) rather than using values derived directly from the trials. The company stated that this was consistent with the approach used in NICE's technology appraisal guidance on CPAP for treating obstructive sleep apnoea. Clinical experts agreed with the company that the EQ-5D may not capture changes in excessive daytime sleepiness. The ERG commented that it is possible that a modest decrease in excessive sleepiness does not significantly impact health-related quality of life. The committee was concerned that if the EQ-5D does not capture quality-of-life benefits adequately in this population, the ESS scores should not be mapped to the EQ-5D, because it will remain insensitive. The committee also noted that the McDaid report stated that the EQ-5D could capture the health effects of sleepiness through its impact on usual activities or anxiety and depression. After technical engagement, the company provided an analysis of mean difference by treatment group using individual patient data from EQ-5D data in the trials. These are academic in confidence and cannot be presented here. The committee considered it uncertain whether the EQ-5D captures quality-of-life benefits in people with obstructive sleep apnoea. In response to consultation, the company

presented evidence from a commissioned study to support the position that the EQ-5D is not sensitive to changes in quality of life for this population. The study investigated 3 metrics that are derivable from the EQ-5D: EQ-INDEX (sum score of the 5 dimensions), EQ-Visual Analogue Scale (EQ-VAS), and z-score (composite of EQ-INDEX and EQ-VAS) in the pitolisant hydrochloride HAROSA trials. The study showed that there was no significant difference in EQ-INDEX for people who had pitolisant hydrochloride and people who had placebo. It also found that the EQ-VAS appeared better correlated with clinical outcomes than the EQ-INDEX. Typically, the larger the EQ-INDEX, or sum of the individual dimensions, the more severe or frequent the problems. However, the study standardised the EQ-INDEX to a 0 to 100 scale and reversed the direction to align with the EQ-VAS, where larger values represent higher reported health. The ERG explained that because the EQ-INDEX was standardised and reversed, it was unknown what the results would have been if EQ-5D utilities based on the UK value set were used. The ERG explained that the study did not provide evidence that EQ-5D utility values are insensitive to changes in quality of life for this population because the EQ-INDEX is not the same as EQ-5D utility values. The company commented that using the EQ-VAS was not an acceptable option within the NICE reference case. The committee was aware that NICE's guide to the methods of technology appraisal states that "in some circumstances the EQ-5D may not be the most appropriate. To make a case that the EQ-5D is inappropriate, qualitative empirical evidence on the lack of content validity for the EQ-5D should be provided, demonstrating that key dimensions of health are missing. This should be supported by evidence that shows that EQ-5D performs poorly on tests of construct validity and responsiveness in a particular patient population. This evidence should be derived from a synthesis of peer-reviewed literature. In these circumstances alternative health-related quality of life measures may be used and must be accompanied by a carefully detailed account of the methods used to generate the data, their validity, and how these methods affect the utility values." The committee concluded that both EQ-5D utility values from the trials and the McDaid approach were relevant for consideration.

An average of the 2 sources of utility values should be used to inform the economic model

3.13 The ERG provided additional scenarios that used an average of 2 sources (the trial EQ-5D utility values and ESS scores mapped to the EQ-5D using the

McDaid approach). The ERG explored 2 methods for averaging the HAROSA and McDaid utilities. The first method averaged the EQ-5D utilities directly from HAROSA with the utilities from McDaid. This approach assumed no relationship between ESS score and EQ-5D in HAROSA. The second method averaged the coefficient of change in ESS score and change in EQ-5D from HAROSA and McDaid. The committee recognised that both methods used novel techniques of determining a utility value using 2 different types of evidence (EQ-5D directly elicited from the trials, and the McDaid mapping approach). However, it understood that the first method took account of any differences in the models used to calculate the utility values (such as covariates). The committee noted the company's approach of assigning utility values was based on both response status and treatment group. It did not consider this approach to be appropriate because there was no evidence provided for a treatment-related difference in quality of life that was not associated with ESS. It agreed that health state utility values based on response status and independent of treatment group would have been preferred. The committee recalled its preference from the first committee meeting for trial EQ-5D values. But it acknowledged that ESS scores mapped using McDaid were also relevant because this was another source of evidence for the change in quality of life associated with ESS. On balance, the committee concluded that the most appropriate source of utility values was uncertain. It agreed that the average of the 2 sources of utility values, using the ERG's first method, should be used to inform the economic model.

A utility decrement for road traffic accidents is not acceptable

3.14 The ERG explained that it agreed to keep the road traffic accidents utility in the original model, on the basis that people taking pitolisant hydrochloride would be more alert when driving. But it noted the utility values for people in slight road traffic accidents appeared too low. So the ERG assumed that people who experienced a slight road traffic accident had a disutility equal to the most severe other event in the model (stroke). It stated that there is no direct evidence to show that pitolisant hydrochloride would reduce the incidence of road traffic accidents because this was not measured in the HAROSA trials. It also stated that the model assumed that people with excessive daytime sleepiness who take pitolisant hydrochloride and drive have the same risk of a road traffic accident as the general population driving in the UK, which is not a plausible assumption. The committee concluded that people with obstructive

sleep apnoea and excessive daytime sleepiness must not drive until their symptoms are under control. So it agreed not to include a utility decrement for road traffic accidents.

Cost-effectiveness estimates

Pitolisant hydrochloride is not a cost-effective use of NHS resources

3.15 The committee considered the cost-effectiveness estimates for pitolisant hydrochloride with and without CPAP, plus standard care, compared with standard care alone. The company provided cost-effectiveness estimates for 2 populations in line with the marketing authorisation. The company's base case adjusted for the Hawthorne effect (using a centring approach) and used utility values derived from ESS scores mapped to EQ-5D using the McDaid approach. For people who have residual excessive daytime sleepiness despite using CPAP, the company's deterministic ICER for pitolisant hydrochloride plus CPAP and standard care, compared with CPAP plus standard care alone, was estimated to be £32,430 per quality-adjusted life year (QALY) gained. For people who declined or could not tolerate CPAP, the ICER for pitolisant hydrochloride plus standard care compared with standard care alone was estimated to be £28,431 per QALY gained. The committee preferred the scenario presented by the ERG, which used the average of 2 sources of utility values: the trial EQ-5D utility values and ESS scores mapped to the EQ-5D using the McDaid approach. For people with residual excessive daytime sleepiness despite CPAP, this increased the ICER to £53,287 per QALY gained. For people who declined or could not tolerate CPAP, the ICER was estimated to be £50,348 per QALY gained. The committee concluded that the most plausible ICER is likely to be above what NICE considers a cost-effective use of NHS resources.

Other factors

People who find CPAP difficult to use are considered in the decision making

3.16 The clinical expert noted that some people with mental health or neurodegenerative conditions may find it challenging to use CPAP regularly, making it difficult to control excessive daytime sleepiness caused by obstructive

sleep apnoea. The marketing authorisation for pitolisant hydrochloride includes people with obstructive sleep apnoea whose excessive daytime sleepiness has not been satisfactorily treated by primary obstructive sleep apnoea therapy, such as CPAP. The committee agreed with the clinical experts that people who find CPAP difficult may be disadvantaged and this was taken into account in its decision making.

Conclusion

Pitolisant hydrochloride is not recommended for treating excessive daytime sleepiness caused by obstructive sleep apnoea

3.17 The committee recognised that excessive daytime sleepiness caused by obstructive sleep apnoea is a debilitating condition that negatively affects many aspects of daily life. It acknowledged that pitolisant hydrochloride with standard care was more effective than standard care alone in reducing excessive daytime sleepiness, as measured by the ESS. The committee noted uncertainty around the utility values used in the model and the placebo effect adjustment. The committee considered that the most plausible cost-effectiveness estimates for pitolisant hydrochloride were above the range that NICE usually considers an acceptable use of NHS resources. Therefore, it did not recommend pitolisant hydrochloride for routine commissioning in the NHS.

4 Appraisal committee members and NICE project team

Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee C.

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.

Anne Murray-Cota and Catie Parker
Technical leads

Christian Griffiths and Caron Jones
Technical advisers

Gavin Kenny
Project manager

ISBN: 978-1-4731-4477-4

Accreditation