

# Ustekinumab for moderately to severely active Crohn's disease after previous treatment

Technology appraisal guidance

Published: 12 July 2017

[www.nice.org.uk/guidance/ta456](https://www.nice.org.uk/guidance/ta456)

## 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.

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## 1 Recommendations

- 1.1 Ustekinumab is recommended, within its marketing authorisation, as an option for treating moderately to severely active Crohn's disease, that is, for adults who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a TNF-alpha inhibitor or have medical contraindications to such therapies.
- 1.2 The choice of treatment between ustekinumab or another biological therapy should be made on an individual basis after discussion between the patient and their clinician about the advantages and disadvantages of the treatments available. If more than 1 treatment is suitable, the least expensive should be chosen (taking into account administration costs, dosage and price per dose).
- 1.3 Ustekinumab should be given until treatment failure (including the need for surgery) or until 12 months after the start of treatment, whichever is shorter. People should then have their disease reassessed in accordance with NICE's recommendations for [infliximab and adalimumab for the treatment of Crohn's disease](#) to see whether treatment should continue.

## 2 The technology

<b>Description of the technology</b>	Ustekinumab (Stelara, Janssen) is a human monoclonal antibody that acts as a cytokine inhibitor by targeting interleukin-12 (IL-12) and interleukin-23 (IL-23).
<b>Marketing authorisation</b>	<p>Ustekinumab has a marketing authorisation in the UK for treating 'adult patients with moderately to severely active Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a TNF-alpha inhibitor or have medical contraindications to such therapies:</p> <ul style="list-style-type: none"> <li>• Patients who have not shown adequate response at 8 weeks after the first subcutaneous dose may receive a second subcutaneous dose at this time.</li> <li>• Patients who lose response on dosing every 12 weeks may benefit from an increase in dosing frequency to every 8 weeks.</li> <li>• Patients may subsequently be dosed every 8 weeks or every 12 weeks according to clinical judgment'.</li> </ul>
<b>Adverse reactions</b>	The most common adverse reactions for ustekinumab include arthralgia, headache, nausea, pyrexia, nasopharyngitis, abdominal pain, upper respiratory tract infection, diarrhoea and fatigue. For full details of adverse reactions and contraindications, see the summary of product characteristics.
<b>Recommended dose and schedule</b>	<p>Ustekinumab is given as intravenous infusion at induction and as subcutaneous injection at maintenance:</p> <ul style="list-style-type: none"> <li>• 1 intravenous induction treatment (dose depends on body weight and is approximately 6 mg/kg).</li> <li>• Maintenance subcutaneous treatment at week 8 (90 mg), then every 12 weeks.</li> </ul>
<b>Price</b>	<p>The list price for ustekinumab is £2,147 per 130-mg vial concentrate for solution for infusion and per 90-mg vial solution for injection (excluding VAT; Monthly Index of Medical Specialties).</p> <p>A confidential pricing arrangement has been agreed with the Commercial Medicines Unit.</p>

### 3 Evidence

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

## 4 Committee discussion

The appraisal committee reviewed the data available on the clinical and cost effectiveness of ustekinumab, having considered evidence on the nature of moderately to severely active Crohn's disease and the value placed on the benefits of ustekinumab by people with the condition, those who represent them, and clinical experts. It also took into account the effective use of NHS resources.

### *Clinical effectiveness*

#### Clinical need of people with Crohn's disease

- 4.1 The committee understood that Crohn's disease follows an unpredictable, relapsing and remitting course with many debilitating symptoms. It heard from the patient experts that the disease can present a major barrier to a person's ability to participate in daily life, severely affecting their self-esteem, social functioning, engagement in work and other activities, personal relationships and family life. The patient experts recounted their experience of current treatments including conventional non-biological therapy and TNF-alpha inhibitors, and their intolerance to, or subsequent loss of response to these treatments. The committee heard that patients fear loss of remission and exacerbations of the disease because of the major impact these have on quality of life. It also heard that it is very important to have a range of treatment options to enable patients to regain remission. The committee noted that both the patient experts had ustekinumab as part of a clinical trial after losing response to TNF-alpha inhibitors. Both recounted a positive response to treatment with ustekinumab and emphasised its life-changing effects, with good control of symptoms allowing them to resume work and everyday activities as well as avoiding the need for surgery. One patient expert explained that ustekinumab had left him feeling 'wonderfully normal again' while the other highlighted the immense improvement to her quality of life, enabling her to start a family. The patient experts also emphasised that maintenance treatment with ustekinumab is a subcutaneous injection rather than an intravenous infusion, which is greatly valued by patients because it means they can take the treatment at home with no need for hospital visits. The committee acknowledged that ustekinumab is a convenient and well-tolerated treatment that has considerably improved the quality of life of the patient experts. It concluded that the availability of a further treatment option to improve symptoms and bring the disease into

remission would be highly valued by people with Crohn's disease.

## Current clinical management of Crohn's disease

- 4.2 The committee heard from the clinical experts that initial treatment for people with Crohn's disease is conventional non-biological treatment but if this fails, patients are offered a TNF-alpha inhibitor (infliximab or adalimumab). If this fails or is unsuitable, patients may switch to an alternative TNF-alpha inhibitor or have vedolizumab in line with NICE technology appraisal guidance on [vedolizumab for treating moderately to severely active Crohn's disease after prior therapy](#). It was the clinical experts' opinion that only when all other options have been exhausted, including dose escalation of a TNF-alpha inhibitor despite it becoming less effective, would various non-biological approaches including surgery be considered. The committee heard from the clinical experts that ustekinumab is a novel treatment with a different mechanism of action to existing treatments, and that it can be used either in place of a TNF-alpha inhibitor after conventional non-biological treatment has failed, or instead of vedolizumab (or a subsequent TNF-alpha inhibitor, for which there is very limited evidence) after a first TNF-alpha inhibitor has failed. It acknowledged that the clinical experts value using TNF-alpha inhibitors first-line, after failure of conventional non-biological treatment, because there is considerable clinical experience in using them. It is likely therefore that ustekinumab would predominantly be used later in the treatment pathway, although there may be some individual patients for whom ustekinumab would be considered earlier. The committee concluded that ustekinumab would be used as an option where other biological treatments would be considered appropriate, and hence that these are the relevant comparators in the appraisal.
- 4.3 The committee considered the duration of treatment with current biological therapies in clinical practice. It heard from the clinical experts that in line with current guidelines the benefit of these agents is assessed after induction to ensure a primary response and then at 1 year to see whether treatment should continue. The clinical experts emphasised that, when there is evidence of clinical benefit, therapy usually continues beyond 1 year in order to avoid complications and exacerbations that can result in life-changing surgery. However, the clinical experts acknowledged that there are currently no clinical data to support the long-term effectiveness of biological therapies. The committee also heard from the clinical experts that evidence from the UK Inflammatory Bowel Disease



Audit shows that most patients continue on biological therapy for more than 1 year and that initial results suggest that continuous use is associated with better outcomes. The committee concluded that there is uncertainty about the appropriate duration of treatment with biological therapy but that evidence from current practice suggests there may be a benefit to continuing treatment beyond 1 year.

## Clinical trial evidence

4.4 The committee noted that the clinical evidence for ustekinumab came from 2 induction trials (UNITI-1 and UNITI-2) and 1 maintenance trial (IM-UNITI) that included patients who had had a clinical response to ustekinumab in either of the 2 induction trials. It was aware that the UNITI-1 and -2 trials were identical in design except for the trial populations. In UNITI-1, patients had had TNF-alpha inhibitor therapy but did not respond, lost response or were intolerant to it ('the TNF-alpha-inhibitor failure population'). In UNITI-2, patients had had conventional non-biological treatment that had failed ('the conventional-care failure population'). The committee noted the evidence review group (ERG's) comments that the induction trials were generally well conducted with high internal validity and were reasonably generalisable to the UK Crohn's disease population, although the committee was aware of some issues worthy of further consideration. For example, clinical advice to the ERG suggested that the Crohn's disease activity index (CDAI; a measurement of clinical, biochemical and physical parameters of disease activity) on which the primary outcome in the trials was based, is not used in clinical practice in the UK. The committee heard from the clinical experts present at the meeting that outcomes based on the CDAI have historically been used in studies of biological treatments in Crohn's disease to assess response, and therefore it was not unreasonable that they were used in the current trials. However they explained that there is now a move towards more objective assessment of disease activity, such as endoscopic evaluation of ulceration. The committee accepted that the use of the CDAI was acceptable given its historic use in assessing response to other biological treatments. The committee also noted that the trial excluded patients with the most severe disease (defined by a CDAI score higher than 450). The committee heard from the clinical experts that the trial populations were generally representative of patients seen in clinical practice and that the exclusion of some groups of patients, such as those with the most severe disease, was a limitation of trials generally. The committee concluded that the

studies were of a good quality and broadly generalisable to the population likely to have ustekinumab in clinical practice in England.

## Clinical effectiveness results from induction trials

4.5 The committee noted that in both of the induction trials, the proportion of patients with a clinical response at 6 weeks (the primary outcome, defined as a reduction from baseline in CDAI score of 100 points or more) was significantly greater in patients randomised to ustekinumab compared with placebo. In UNITI-1, 33.7% of patients in the ustekinumab group at the licensed dose of approximately 6 mg/kg had a clinical response compared with 21.5% in the placebo group ( $p=0.003$ ). In UNITI-2, 55.5% of patients in the ustekinumab group had a clinical response compared with 28.7% in the placebo group ( $p=0.001$ ). The committee also noted that there were statistically significant differences between ustekinumab and placebo in the rates of clinical remission (defined as attaining a CDAI score of less than 150 points) and other secondary outcomes. The committee noted that the results were more favourable for the conventional-care failure population in UNITI-2 than for the TNF-alpha-inhibitor failure population in UNITI-1. However, it understood from the clinical experts that patients in whom TNF-alpha inhibitors have failed are likely to respond less well to all biological treatments than patients who are naive to TNF-alpha inhibitors. The committee concluded that the results from the induction studies suggest that ustekinumab is associated with higher rates of response and clinical remission compared with placebo in both populations of patients.

## Clinical effectiveness results from maintenance trials

4.6 The committee noted that at 44-week follow-up in the IM-UNITI maintenance trial, the proportion of patients in clinical remission (the primary outcome) was significantly greater in both the 90 mg every 12 weeks (48.8%) and 90 mg every 8 weeks (53.1%) ustekinumab groups than in the placebo group (35.9%,  $p=0.040$  and  $p=0.005$  respectively). It also noted that there were statistically significant differences between ustekinumab and placebo for clinical response at 44 weeks. The committee acknowledged that the company had submitted some additional results up to week 92 but that no statistical comparisons between ustekinumab and placebo were presented. It concluded that the results from the maintenance study suggest that ustekinumab is associated with higher rates of clinical remission and response at 44 weeks compared with placebo but that

the longer-term effects are uncertain because limited data are available.

## Relative effectiveness of ustekinumab and other biological therapies

- 4.7 The committee noted that the company had presented indirect comparisons to provide comparative efficacy estimates for ustekinumab compared with other biological treatments. It understood that analyses were performed separately for induction trials and maintenance trials and for the conventional-care failure population and the TNF-alpha-inhibitor failure population. For the induction phase, the company provided a network meta-analysis. The committee noted that the ERG considered that the trials included in the network meta-analysis were generally conducted to a high-standard. However there were some limitations with the analysis because of variability in the time at which primary outcomes were assessed in the trials and differences in treatment history and previous exposure to TNF-alpha inhibitors. It also noted that only 1 small study of infliximab was included in the analysis and that the company had highlighted the need to interpret the results of the study with caution because of missing data, and because a smaller magnitude of effect was observed with higher doses of infliximab than with smaller doses. The committee acknowledged that the network meta-analysis suggested significantly higher rates of response and remission in the induction phase with infliximab compared with ustekinumab but no statistically significant differences between ustekinumab and the other biological therapies. However, it concluded that the results were associated with uncertainty and that the comparison between infliximab and ustekinumab in particular should be interpreted with caution.
- 4.8 For the maintenance phase, the company carried out a treatment sequence analysis instead of a conventional network meta-analysis because of the multiple sources of heterogeneity between the maintenance trials. The committee noted that the company's aim was to evaluate treatment effects over the entire treatment sequence to reduce bias inherently associated with the analysis of long-term relative treatment effect estimates for ustekinumab. The committee also noted that the company stated that this was a complex analysis and the results should be viewed with caution. The committee was aware that the ERG had identified a number of issues with the company's analysis, and believed the results were highly uncertain. The ERG's concerns included the comparability of the trials included in the treatment sequence analysis. It also considered that the methods used to construct the control arm for biological

therapies had considerable potential for confounding of results, because the analysis was based on placebo-data from IM-UNITI and not on randomised comparisons. The committee acknowledged that both the company and the ERG had reservations about the reliability of the treatment sequence analysis. It agreed that the treatment sequence analysis had many limitations and that the results should be interpreted with caution.

## *Cost effectiveness*

### **Company's economic model**

- 4.9 The company presented a model consisting of a short-term induction phase (a decision tree) and a long-term maintenance phase (a Markov state transition model) comparing ustekinumab with conventional non-biological therapies and other biological therapies (infliximab, adalimumab and vedolizumab) in patients with moderately to severe active Crohn's disease. The committee recalled that ustekinumab would be used in place of other biological treatments (see [section 4.2](#)) and therefore the comparison of ustekinumab with other biological treatments is the most relevant to the appraisal.
- 4.10 The committee acknowledged comments from the ERG about the general weaknesses of the model structure. It heard that it did not fully characterise the chronic life-long relapsing-remitting nature of Crohn's disease because it did not allow patients to cycle through multiple biological therapies. It also heard that the impact of surgery on future prognosis, including the need for further surgery, and health-related quality of life were not appropriately incorporated. The committee acknowledged that similar models had been used in other technology appraisals for Crohn's disease and, while noting its limitations, concluded that the structure of the model was acceptable for decision making. However it also noted the ERG's comment that research is needed to develop a new and more appropriately structured decision-analytic model for Crohn's disease, which could be used in future appraisals.

### **Cost-effectiveness results**

- 4.11 The committee noted that in the company's base-case analysis ustekinumab dominated other biological treatments (that is, it cost less and resulted in higher quality adjusted life years [QALYs]), both in the conventional-care failure population and in the TNF-alpha-inhibitor failure population. It also noted that

ustekinumab remained dominant compared with other biological treatments in the ERG's exploratory analyses using the company's model structure. The committee observed that there were only small differences in the QALY estimates between the different biological therapies as estimated by the company and the ERG. It recognised that this leads to instability in the cost-effectiveness results and therefore further considered the company's suggestion that a cost-minimisation analysis may be more appropriate. The committee heard from the ERG that it is not unreasonable to assume similar efficacy between the biological therapies based on the available evidence. It also recalled that the clinical experts had commented that the absence of direct comparative data meant that it was unknown whether there were any differences in efficacy. The committee was therefore persuaded that cost minimisation was not an unreasonable approach. It noted that in the company analysis, which used the confidential pricing arrangement for ustekinumab agreed with the Commercial Medicines Unit, ustekinumab appeared to have lower total costs in year 1 than comparator treatments when considered at their list price, and therefore ustekinumab could be considered a cost-effective option for use in the NHS. However, the committee was mindful that different prices may be available in the NHS for different biological treatments and it concluded that the total cost of the treatments should be taken into account when deciding which one to use in clinical practice.

## Innovation

- 4.12 The committee discussed the innovative aspects of ustekinumab, recognising that it offered less frequent dosing in the maintenance stage than the other biological treatment administered by subcutaneous injection. The committee accepted that the positive impact this can have on minimising the interruption of patients' daily living, including work activities, may not be fully captured in the cost-effectiveness modelling. The committee concluded that ustekinumab is an innovative and cost-effective treatment for treating moderately to severely active Crohn's disease and should be recommended for use in the NHS.

## *Pharmaceutical Price Regulation Scheme (PPRS) 2014*

- 4.13 The committee was aware of NICE's position statement on the Pharmaceutical Price Regulation Scheme (PPRS) 2014, and in particular the PPRS payment mechanism. It accepted the conclusion 'that the 2014 PPRS payment

mechanism should not, as a matter of course, be regarded as a relevant consideration in its assessment of the cost effectiveness of branded medicines'. The committee heard nothing to suggest that there is any basis for taking a different view about the relevance of the PPRS to this appraisal. It therefore concluded that the PPRS payment mechanism was not relevant in considering the cost effectiveness of the technology in this appraisal.

### Summary of appraisal committee's key conclusions

TA456	Appraisal title: Ustekinumab for moderately to severely active Crohn's disease after previous treatment	Section
<b>Key conclusion</b>		
<p>Ustekinumab is recommended, within its marketing authorisation, as an option for treating moderately to severely active Crohn's disease, that is, for adults who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a TNF-alpha inhibitor or have medical contraindications to such therapies.</p> <p>The committee concluded that the results from the ustekinumab studies suggest that it is associated with higher rates of response and clinical remission compared with placebo.</p> <p>The committee considered that the company's treatment sequence analysis comparing ustekinumab with other biological treatments had many limitations and that the results should be interpreted with caution.</p> <p>The committee was persuaded that cost minimisation was not an unreasonable approach. It noted that in the company analysis, which used the confidential pricing arrangement for ustekinumab agreed with the Commercial Medicines Unit, ustekinumab appeared to have lower total costs in year 1 than comparator treatments when considered at their list price, and therefore ustekinumab could be considered a cost-effective option for use in the NHS.</p>		<p>1.1, 4.5, 4.8, 4.11</p>
<b>Current practice</b>		

Clinical need of patients, including the availability of alternative treatments	The committee acknowledged that ustekinumab is a convenient treatment that had considerably improved the quality of life of the patient experts. It concluded that the availability of a further treatment option to improve symptoms and bring the disease into remission would be highly valued by people with Crohn's disease.	4.1
<b>The technology</b>		
Proposed benefits of the technology How innovative is the technology in its potential to make a significant and substantial impact on health-related benefits?	The committee concluded that ustekinumab is an innovative and cost-effective treatment.	4.12
What is the position of the treatment in the pathway of care for the condition?	The committee concluded that ustekinumab would be used in place of other biological treatments and hence that these are the relevant comparators in the appraisal.	4.2
Adverse reactions	The committee acknowledged that ustekinumab is a well-tolerated treatment.	4.1
<b>Evidence for clinical effectiveness</b>		
Availability, nature and quality of evidence	The committee noted that the clinical evidence for ustekinumab came from 2 induction trials (UNITI-1 and UNITI-2) and 1 maintenance trial (IM-UNITI) that included patients who had had a clinical response to ustekinumab in either of the 2 induction trials. The committee concluded that the studies were of a good quality.	4.4

Relevance to general clinical practice in the NHS	The committee concluded that the studies were broadly generalisable to the population likely to have ustekinumab in clinical practice in England.	4.4
Uncertainties generated by the evidence	<p>The committee concluded that there is uncertainty about the appropriate duration of treatment with biological therapy but that evidence from current practice suggests there may be a benefit to continuing treatment beyond 1 year.</p> <p>The committee considered that the company's treatment sequence analysis comparing ustekinumab with other biological treatments should be interpreted with caution.</p>	4.3, 4.8
Are there any clinically relevant subgroups for which there is evidence of differential effectiveness?	The committee noted that the results were more favourable for the conventional-care failure population in UNITI-2 than for the TNF-alpha-inhibitor failure population in UNITI-1. However, it understood from the clinical experts that patients in whom TNF-alpha inhibitors have failed are likely to respond less well to all biological treatments than patients who are naive to TNF-alpha inhibitors.	4.5
Estimate of the size of the clinical effectiveness including strength of supporting evidence	The committee concluded that the results from the ustekinumab studies suggest that it is associated with higher rates of response and clinical remission compared with placebo.	4.5, 4.6
<b>Evidence for cost effectiveness</b>		



<p>Availability and nature of evidence</p>	<p>The company presented a model consisting of a short-term induction phase (a decision tree) and a long-term maintenance phase (a Markov state transition model) comparing ustekinumab with conventional non-biological care and other biological therapies (infliximab, adalimumab and vedolizumab) in patients with moderately to severe active Crohn's disease. The committee recalled that ustekinumab would be used in place of other biological treatments and hence that the comparison of ustekinumab with other biological treatments is the most relevant to the appraisal.</p>	<p>4.9</p>
<p>Uncertainties around and plausibility of assumptions and inputs in the economic model</p>	<p>The committee acknowledged comments from the ERG about the general weaknesses of the model structure.</p>	<p>4.10</p>
<p>Incorporation of health-related quality-of-life benefits and utility values  Have any potential significant and substantial health-related benefits been identified that were not included in the economic model, and how have they been considered?</p>	<p>The committee accepted that the positive impact of the reduced administrative burden of ustekinumab in the maintenance phase, minimising the interruption of patients' daily living and work activities, may not be fully captured in the cost-effectiveness modelling.</p>	<p>4.12</p>

Are there specific groups of people for whom the technology is particularly cost effective?	None.	-
What are the key drivers of cost effectiveness?	The committee was persuaded that cost minimisation was not an unreasonable approach.	4.11
Most likely cost-effectiveness estimate (given as an ICER)	The committee noted that in the company's cost-minimisation analysis, which used the confidential pricing arrangement for ustekinumab agreed with the Commercial Medicines Unit, ustekinumab appeared to have lower total costs in year 1 than comparator treatments when considered at their list price, and therefore ustekinumab could be considered a cost-effective option for use in the NHS. However the committee was mindful that different prices may be available in the NHS for different biological treatments and it concluded that the total cost of the treatments should be taken into account when deciding which one to use in clinical practice.	4.11
<b>Additional factors taken into account</b>		
Patient access schemes (PPRS)	The contract prices used for decision-making in this appraisal are the relevant prices the NHS pays for ustekinumab. These prices are based on contract pricing arrangements between the company and the Commercial Medicines Unit.	5.4
Equalities considerations and social value judgements	No equalities issues were identified.	-

## 5 Implementation

- 5.1 Section 7(6) of the [National Institute for Health and Care Excellence \(Constitution and Functions\)](#) and the [Health and Social Care Information Centre \(Functions\) Regulations 2013](#) requires clinical commissioning groups, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.
- 5.2 The Welsh Assembly Minister for Health and Social Services has 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 3 months of the guidance being published.
- 5.3 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 moderately to severely active Crohn's disease and the doctor responsible for their care thinks that ustekinumab is the right treatment, it should be available for use, in line with NICE's recommendations.
- 5.4 The contract prices used for decision-making in this appraisal are the relevant prices the NHS pays for ustekinumab. These prices are based on contract pricing arrangements between the company and the Commercial Medicines Unit. The contract prices are commercial in confidence. Any enquiries from NHS organisations about the contract prices used in this appraisal should be directed to the Commercial Medicines Unit.

## 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 A](#).

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

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

### *NICE project team*

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

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ISBN: 978-1-4731-2588-9

## Accreditation

