

**NATIONAL INSTITUTE FOR HEALTH AND CARE
EXCELLENCE**

Appraisal consultation document

Chlormethine gel for treating mycosis fungoides-type cutaneous T-cell lymphoma

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using chlormethine gel 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 chlormethine gel 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: 11 February 2021

Third appraisal committee meeting: TBC

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

1 Recommendations

- 1.1 Chlormethine gel is not recommended, within its marketing authorisation, for treating mycosis fungoides-type cutaneous T-cell lymphoma (MF-CTCL) in adults.
- 1.2 This recommendation is not intended to affect treatment with chlormethine gel 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

Most treatments for early MF-CTCL aim to relieve the skin symptoms. Options depend on the extent of the skin affected, but may include treatments applied to the skin, such as topical steroids, phototherapy (light therapy) and radiotherapy. Systemic treatment that targets the whole body, such as oral bexarotene, can also be used to relieve skin symptoms if those treatments do not work, no longer work, or become unsuitable.

Clinical evidence shows that chlormethine gel improves skin disease. It may be particularly beneficial for people who have skin disease over a limited area of the body or for whom phototherapy is unsuitable. However, there is no robust evidence for its effectiveness compared with other treatments or showing if it's more effective for people with limited skin disease.

The evidence used to estimate cost effectiveness is uncertain because it does not accurately reflect clinical practice. Other areas of uncertainty include:

- the true effectiveness of phototherapy, which was used as a comparator in the model
- how long skin symptoms respond to treatment
- the amount of chlormethine gel used per day.

The cost effectiveness estimates were also based on a treatment sequence that people do not have in clinical practice. Because of this and the uncertainties around the evidence, the cost-effectiveness estimates are not reliable. The estimates using the preferred assumptions are above what NICE considers a cost-effective use of NHS resources. Therefore, chlormethine gel is not recommended.

2 Information about chlormethine gel

Marketing authorisation indication

- 2.1 Chlormethine gel (Ledaga, Recordati Rare Diseases and Helsinn Healthcare) is indicated for 'the topical treatment of mycosis fungoides-type cutaneous T-cell lymphoma (MF-type CTCL) in adult patients'.

Dosing in the marketing authorisation

- 2.2 The dosage schedule is available in the [summary of product characteristics](#).

Price

- 2.3 The list price for chlormethine gel is £1,000 per 60 g tube (excluding VAT; BNF online accessed 17 July 2020).
- 2.4 The company has a commercial arrangement (simple discount patient access scheme). This makes chlormethine gel available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

3 Committee discussion

The appraisal committee (section 5) considered evidence submitted by Recordati Rare Diseases and Helsinn Healthcare, a review of this submission by the evidence review group (ERG), the technical report, and responses from stakeholders. See the [committee papers](#) for full details of the evidence.

The appraisal committee was aware that several issues were resolved during the technical engagement stage, and agreed that:

- Phototherapy (PUVA and UVB bundled) is an appropriate comparator for chlormethine gel in the model.
- The company's estimate for phototherapy administration costs is acceptable for use in the model. Costs were derived from the mean of dermatology and oncology costs for consultant-led outpatient clinic cost of phototherapy and photochemotherapy (sourced from NHS reference costs 2017/18). The company and the ERG agreed that the PROCLIP registry is an appropriate source of evidence to derive the distributions of PUVA and UVB phototherapy for the model.
- The Kim 2003 study is an acceptable data source to estimate time to progression to systemic treatment after a complete skin symptom response on chlormethine gel in the model. Study 201 is the current best available evidence for estimating complete and partial response rates in the chlormethine gel arm of the model. The company agreed with the ERG to use Phan et al. 2019 as the data source for complete and partial response rates in the phototherapy arm of the model.

Clinical need

There is a clinical need for chlormethine gel as an alternative treatment option for people with MF-CTCL, particularly in people with low skin burden

3.1 The patient expert explained in their written statement that mycosis fungoides-type cutaneous T-cell lymphoma (MF-CTCL) negatively affects many aspects of life including employment, leisure activities, relationships and day-to-day living. It can also have a psychosocial effect. Symptoms include itching, pain and fever, which can be distressing and are associated with fatigue, anxiety and depression. There is often a delay in being diagnosed with MF-CTCL, and people may already have tried several treatments to relieve their skin symptoms before their eventual diagnosis. The effects of skin-directed treatments, including phototherapy and sometimes radiotherapy, are not long lasting and people often cycle

between treatments. This means people must travel for repeated hospital appointments and quality of life may be affected. A new option which could be used at home would be welcomed. People with early disease (which consists of patches or plaques on the skin but no disease elsewhere in the body) have a particular unmet need because existing treatments are limited. Clinical experts noted that they may be offered topical steroids or emollients, but these only relieve the symptoms of itchiness and redness and do not reduce the patches or plaques. The only options for treating the patches are localised radiotherapy, which is not ideal for younger people, and phototherapy. There is a particular disadvantage of phototherapy for people with limited skin disease (disease covering less than 10% of the skin surface), because the whole skin is exposed to the UV radiation, which carries a long-term risk of inducing skin cancer. These people would prefer an effective topical treatment applied only to the disease area. The committee also recognised the need for an alternative treatment option that may be more convenient and could be particularly useful during the COVID-19 pandemic. It concluded that chlormethine gel would be particularly useful for people who have limited skin disease to avoid whole body phototherapy, or people for whom phototherapy is not effective or who have exceeded the maximum safe UV exposure for phototherapy. It could also be helpful for those who find it difficult to attend hospital for courses of phototherapy.

Treatment pathway

Chlormethine gel relieves skin symptoms but is not a cure

3.2 Clinical experts explained that, in practice, chlormethine gel would be prescribed for up to a year, probably in the first instance for 4 to 6 months, then reassessed. Treatment would stop if the skin disease resolves. For people with a partial response in skin symptoms, treatment would be expected to stop after a year. People could have further courses of treatment with chlormethine gel, or move onto other skin-directed

treatments, such as phototherapy, if the chlormethine gel was not effective. Clinical experts also explained that like the other skin-directed treatments available for MF-CTCL, chlormethine gel is not a cure, and does not affect the spread of the disease to other organs in the body or mortality from the disease. However, if the skin disease cannot be controlled, people are offered systemic therapy even if the disease has not spread to other areas, so keeping the skin disease under control is important. If another skin-directed therapy were available, it could keep the skin disease under control for longer. The clinical experts explained that there was a previous similar version of this treatment in the form of a nitrogen mustard ointment. The committee understood that people had benefited from treatment with nitrogen mustard, and that up until recently it was still being used in parts of the UK. The clinical experts explained that, although it is uncommon for skin symptoms to completely resolve, therapies can relieve skin symptoms and improve people's quality of life. The committee concluded that chlormethine gel is not a disease-modifying treatment, but it relieves skin symptoms and improves quality of life.

People with early stage MF-CTCL have multiple treatments

3.3 Clinical experts explained that skin-directed therapy decisions for MF-CTCL are based on the extent of the skin involvement, not just the overall stage of disease. In practice, people with advanced MF-CTCL (stage 2B to 4) who have disease at sites other than the skin, and are having chemotherapy, could still have skin lesions that might benefit from chlormethine gel. As noted in section 3.1, for people with early stage disease and a low skin burden (less than 10%; typically stage 1A but other stages may also have low skin burden) have a particular unmet need because of the disadvantages of whole body phototherapy when the extent of the disease is limited. People with early stage disease and a skin burden greater than 10% of body surface area (typically stage 1B but other stages may also have high skin burden) are usually offered topical treatments, phototherapy or localised radiotherapy. The clinical experts explained that people with early stage MF-CTCL, whose disease is

confined to the skin, cycle through available treatments, with the sequence depending on the response in skin symptoms. Because individual treatments are typically not long lasting, multiple courses of treatment are usually necessary, although the number of courses of phototherapy is limited by the cumulative UV dose. It is therefore likely that repeated courses of chlormethine gel would be offered, and in practice phototherapy could be followed by chlormethine gel or vice versa. If the skin disease becomes refractory to skin-directed treatments, or the maximum safe UV exposure has been reached, or if the condition progresses to an advanced stage, systemic therapies such as oral bexarotene and peginterferon alfa are offered. The committee concluded that treatment in clinical practice depends on the level of skin burden and the extent of the underlying disease. But in practice people with early MF-CTCL have multiple treatments in different sequences until symptoms no longer respond or the disease spreads beyond the skin.

Clinical evidence

The main trial shows chlormethine gel improves the skin symptoms of early stage MF-CTCL but compares it with a treatment that is no longer used

3.4 The main trial, Study 201, was a non-inferiority trial (a trial showing that a new treatment is not substantially worse than another treatment) comparing chlormethine gel with chlormethine ointment in 260 people with early stage MF-CTCL (stage 1A to 2A). Skin symptom response rate was scored on the Composite Assessment of Index Lesion Severity (CAILS) and the modified Severity Weighted Assessment Tool (mSWAT). The overall response rate for chlormethine gel was 58.5% using CAILS and 46.9% using mSWAT. Using CAILS, 13.8% of people had a complete response in skin symptoms and 44.6% of people had a partial response in skin symptoms. The complete and partial response rates measured using mSWAT are confidential and cannot be reported. The committee understood that Study 201 shows that chlormethine gel improves the skin

symptoms of early stage MF-CTCL. However, because the comparator ointment is no longer used in clinical practice, the committee concluded that Study 201 does not show how effective chlormethine gel is compared with standard care. Moreover, no advanced stage patients were included in the trial so the effectiveness in people who have advanced disease or are also on chemotherapy is not known.

The clinical effectiveness of chlormethine gel in people with low skin burden or who cannot have phototherapy is not known

3.5 Clinical experts highlighted that treatment in clinical practice is typically based on the level of skin involvement. They said that people with stage 1A disease or a low skin burden may benefit most because phototherapy involves unnecessary whole body UV exposure (see section 3.1). The trial evidence presented by the company was in early stage MF-CTCL (stage 1A to 2A). While the company submission reported the mean skin burden of the participants, as well as the mean body surface area, response rates were not stratified based on the level of skin disease at baseline. The committee concluded there was no evidence presented to allow it to judge how effective chlormethine gel would be in people:

- with limited skin disease who prefer not to have phototherapy because of the risk of skin cancer
- for whom phototherapy is unsuitable, for example because they have exceeded the safe maximum dose.

The clinical effectiveness of chlormethine gel compared with phototherapy is not known

3.6 The company compared phototherapy with chlormethine gel in its submission. However, there was no evidence directly comparing chlormethine gel with phototherapy and no connected network for an indirect comparison could be formed. Therefore the company did an unadjusted naive comparison. However, most of the studies available to

provide estimates of phototherapy's effectiveness are of low quality and there was considerable debate about the most appropriate source used. The company initially used overall response rates from the weighted average estimates of 7 phototherapy studies. But it then used results from a systematic review on the clinical effectiveness of phototherapies (Phan et al. 2019) identified by the ERG in its base case after technical engagement. The response rates in the 7 studies identified by the company and in the systematic review were higher for phototherapy than the response rates for chlormethine gel in Study 201. Complete skin symptom response was also higher for phototherapy than partial skin symptom response (73.2% compared with 20.8%, as reported in the 7 phototherapy studies), but the reverse was the case for chlormethine gel (13.8% compared with 44.6% using CAILS). The clinical experts said that the reason the response rates in Study 201 appeared lower than the phototherapy trials is that Study 201 used clear criteria for assessing response (CAILS and mSWAT), whereas most of the phototherapy trials were based on less reliable assessments by clinicians. Responses to consultation noted that the early studies of chlormethine in ointment form, which are all retrospective studies, had response rates comparable to those from the phototherapy studies. They suggested that the lower response rates in Study 201 may be because many patients (39%) in the trial had already had phototherapy. The committee understood that most studies included in Phan et al. 2019 were retrospective and at risk of bias. It also noted the ERG's concern that there was substantial heterogeneity across the included studies, including differences in how complete and partial response in skin symptoms were defined and measured. The committee concluded that the true clinical effectiveness of chlormethine gel compared with phototherapy is not known, given the high uncertainty associated with the unadjusted naive comparison.

Cost effectiveness

Clinical practice is better represented in the company's updated model than the original, simplified model

3.7 The company substantially updated its model in response to consultation to try to better reflect the treatment pathway for people with MF-CTCL in clinical practice. As part of these changes, the base case was adjusted so that the time horizon of the model was 20 years instead of a lifetime horizon. The ERG considered that the shorter time horizon was appropriate and captured all the relevant costs and quality-adjusted life year (QALY) implications of a decision to treat with chlormethine gel or phototherapy. The company also introduced a watch and wait state in its updated model for people who have an initial complete response. This was after patient input that, for people whose skin disease progressed after treatment, but whose symptoms are limited and are not affecting their functioning, a watch and wait approach is typical in practice before resuming treatment. The ERG agreed that introducing this state more accurately reflected the clinical pathway. Clinical experts at the second meeting also noted that in clinical practice if people relapse after treatment, they may not be offered further treatment right away. Some may enter the watch and wait state until their skin symptoms return to their original severity before starting another treatment. The committee concluded that the company's updated model better reflected clinical practice than the overly simplistic original model.

Treatment sequencing for refractory skin symptoms in clinical practice is not reflected in the updated model

3.8 In the company's updated model, people whose skin disease does not respond to treatment (refractory disease) may have additional courses of chlormethine gel or phototherapy in a new state: skin-directed therapy. The ERG considered the addition of the new state to be

reasonable and better reflect clinical practice. However, only people whose condition was refractory to chlormethine gel could enter this new skin-directed therapy state, while people whose condition was refractory to phototherapy proceeded straight to systemic therapy. The ERG considered that this gave chlormethine gel an unfair advantage. The ERG amended the model so that people with disease refractory to chlormethine gel or phototherapy proceeded to systemic treatment, and those in the chlormethine arm had 1 course of phototherapy before moving on to systemic treatment. The committee agreed with the ERG and concluded that the company's model did not accurately reflect what happens in clinical practice for people whose condition was refractory to treatment.

Treatment sequencing for disease that relapses after initial response is not reflected in the updated model

- 3.9 In the company's updated model, if skin symptoms respond to initial treatment but then return, people in the phototherapy arm are offered a second round of phototherapy. In the chlormethine gel arm, if skin symptoms return after initial treatment 80% are offered a second round of chlormethine gel and the other 20% phototherapy. The ERG considered it likely that everyone whose disease responded to chlormethine gel would be offered it again. Clinical expert advice was that if skin symptoms respond (fully or partially) to a particular treatment, the person will usually continue to be offered retreatment with the same treatment until their condition stops responding or, if the treatment is phototherapy, until it becomes unsuitable. If the response to treatment was for a very short time, they may be offered an alternative. The clinical experts also noted that in clinical practice, if only a very limited amount of skin disease reappears, it may not need immediate retreatment, and could take some time to go back to the original pretreatment level. The clinical expert noted that the definition of relapse has not been agreed in clinical practice or research. The committee noted that the ERG's model suggested that using a

treatment for a second time was less effective than the first time, based on the ERG's clinical expert's view that it was not plausible that the response would be the same for subsequent rounds of treatment. But the clinical experts who attended the meeting noted that, if people have minimal skin disease in particular, it does tend to respond as well to repeated retreatments as it did the first time. The clinical experts noted that there is likely to be a biological mechanism of action but this has not been proven. The committee concluded that the ERG's amended model structure better reflected the sequential use of chlormethine gel. However, the committee did not accept the ERG's assumption of reduced efficacy of treatment second time.

The phototherapy effectiveness parameters used in the model are highly uncertain: a consistent data source is preferred

- 3.10 The committee noted that the high levels of uncertainty about the true clinical effectiveness of phototherapy (see section 3.6) made the benefits of chlormethine gel compared with phototherapy in the model uncertain. After technical engagement, the company used data from Phan et al. (2019) for complete response, partial response and progressed disease. But for duration of complete response, the company preferred Whittaker et al. (2012), which reports less optimistic response rates than Phan et al. It is also controlled, prospective, and used an objective scoring system. In response to consultation, the company used retrospective data from the PROCLUPI registry for response rates to do a scenario analysis because it is based in the UK so more generalisable to the NHS, and it uses the same outcome measures as Study 201 (mSWAT). The ERG was concerned about the quality of all sources of data for the effectiveness of phototherapy. It was particularly concerned with the company's use of Whittaker et al. (2012) because it had a small sample size and excluded people with stage 1A disease. The ERG preferred to use Phan et al. (2019) for all outcome measures because it ensured the same, consistent source of data for response rates and duration, reducing potential bias, and

because it separates outcomes by type of phototherapy and stage of disease. The committee accepted that there were some real-world UK data available from the PROCLIP registry. Although these were potentially relevant, there were no data from the registry for duration of response, which is needed for modelling. The committee acknowledged the uncertainty around capturing the effectiveness of phototherapy in the model, given the poor data available. It concluded that the true clinical effectiveness of phototherapy was not known and that, although it did not consider that any data source was robust, it preferred the ERG's approach of using 1 data source for all outcome measures.

The mean daily dose of chlormethine gel is uncertain

- 3.11 The clinical experts explained that the amount of gel used depends on skin burden, not disease stage. The committee noted that the population included in the trial had mixed skin burdens, which made it difficult to accurately estimate gel usage. Dose estimates from the clinical experts, the company model, and the ERG were all different. The ERG used a mean daily dose of 2.8 g in the original model. It sourced this information from the summary of product characteristics for Valchlor (the US brand name of chlormethine gel) from Study 201. The company used a lower mean daily dose in their original model, which was taken from individual patient data based on the number of returned empty tubes per follow-up visit from Study 201. The clinical experts estimated that people with limited disease need at least 6 tubes a year (1 every 2 months) because of the shelf-life of the product. But they said it was not uncommon for people to use 1 tube every month with a mean daily dose of approximately 1 g, up to 2 g. They added that usage was difficult to predict and relates to the body surface area affected. The ERG was concerned that the company may have miscalculated how much chlormethine gel was used in the trial, and therefore the cost. For example, the company's estimate did not account for people not returning tubes in Study 201, or not attending follow-up appointments. This may have led to an underestimate of drug

usage. The ERG also considered that the company's calculation of mean daily dose assumes that it was used over a full year. This would underestimate the daily dose if someone used it for less than a year. Basing daily dose on actual time on treatment pushes up the average daily cost. The committee noted that the company and the ERG both sourced their dose estimates from Study 201 and there was no evidence that the ERG estimate was not correct. The committee noted that the ERG took the usage estimates for low and high skin burden from the same source for their 2.8 g estimate, as suggested by the company in response to consultation. The committee concluded that the average daily dose of chlormethine gel, and therefore the costs, were uncertain but preferred the ERG's estimate of 2.8 g.

The committee would have preferred utility values derived from patient-reported outcomes

- 3.12 The company generated utility values from a de novo vignette study and used EQ-5D-5L responses from clinicians, mapped to EQ-5D-3L and valued using the UK general population time-trade off tariffs. The committee understood that chlormethine gel does not aim to cure, but to relieve the skin symptoms of people and improve quality of life. The committee considered patient-reported outcomes important in assessing quality-of-life benefits. The committee concluded that it would have preferred patient-reported outcomes to responses from clinicians to be used for deriving health state utility values.

Cost-effectiveness estimates

Chlormethine gel is unlikely to be cost-effective

- 3.13 There are patient access schemes for chlormethine gel (agreed after the first appraisal consultation document) and for the subsequent treatment bexarotene. Therefore all costs and incremental cost-effectiveness ratios are confidential and cannot be presented. The base-case cost-effectiveness estimates varied greatly between the company and the

ERG, and the committee noted how sensitive the model was to changes in some of the parameters. Incremental QALYs ranged from 0.07 to 0.33 in different scenario analyses. The cost-effectiveness estimates for the whole population with MF-CTCL were considerably above the range normally considered cost effective by NICE, taking into account the committee's preferences for the ERG's:

- amended model structure
- consistent approach of using Phan et al. for all outcome measures for the effectiveness of phototherapy, accepting that this was not a completely reliable source of evidence
- use of 2.8 g for the mean daily dose of chlormethine gel.

Taking into account the limitations of the model structure and uncertainties in the parameters, the committee concluded that there were no reliable cost-effectiveness estimates, and those that included its preferred assumptions were above the acceptable range. It concluded that this suggested that chlormethine gel could not be considered a cost-effective use of resources for the whole MF-CTCL population.

The company does not present any cost-effectiveness analyses by subgroups who may benefit more from chlormethine gel

- 3.14 The clinical experts said in clinical practice treatment depends on the level of skin involvement. They said that people with a low skin burden (typically stage 1A) may benefit most from treatment with chlormethine gel. They have a particular unmet need because the disadvantages of phototherapy are greater for them (see section 3.1). They also need less gel than people with a high skin burden, with potentially lower cost. The clinical experts also noted that for people with a high skin burden, their skin symptoms often do not appear to respond as well to skin-directed treatments. The committee questioned why the company's submission did not separate results by skin burden, by stage, or even by early and advanced disease, except in a scenario analysis. The

committee also noted that combining different levels of skin disease and advanced and early disease added to the uncertainty in costs, both in the amount of chlormethine gel used and the cost of systemic treatment for those who had systemic disease. The committee concluded that the company's model, which is for the whole population, does not reflect clinical practice for people who may benefit the most from chlormethine gel, and adds uncertainty to the cost-effectiveness estimates.

Conclusion

Chlormethine gel is not recommended for treating MF-CTCL

3.15 The committee acknowledged that there is a clinical need for chlormethine gel as an alternative treatment option. It acknowledged that it may benefit people with MF-CTCL, particularly those who have limited disease or who cannot have phototherapy. But the model structure did not reflect the clinical treatment pathway for people with the condition. And no evidence was presented on chlormethine gel's clinical effectiveness for people who have limited disease or who cannot have phototherapy, so the committee could not make a decision on this subgroup. Chlormethine gel's clinical effectiveness relative to phototherapy, which was the focus of the submission, was also unknown. Comparison of symptom response rates from Study 201 and the phototherapy trials used in the model suggested that chlormethine gel may be less effective than phototherapy for treating skin symptoms. But the results from the company's and ERG's models predicted that chlormethine gel is associated with more QALYs than phototherapy, albeit the range in QALY gains was wide. There were other uncertainties, including about the assumptions of the duration of response, and the dosage of chlormethine gel. Because of this high level of uncertainty, and because the committee's preferred scenario estimates were considerably higher than what NICE would usually consider as cost effective, the committee was unable to recommend chlormethine gel for treating MF-CTCL.

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 on information gathered by NICE, and in consultation with consultees and commentators.

Jane Adam

Chair, appraisal committee

January 2021

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 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.

Heather Stegenga and Faye Sheldon

Technical leads

Joanna Richardson and Yelan Guo

Technical advisers

Thomas Feist

Project manager

ISBN: [to be added at publication]