NICE National Institute for Health and Care Excellence

NICE guidance

# Certolizumab pegol for treating rheumatoid arthritis after inadequate response to a TNF-alpha inhibitor

Technology appraisal guidance
Published: 26 October 2016

www.nice.org.uk/guidance/ta415

# 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 is 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.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

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 Certolizumab pegol, in combination with methotrexate, is recommended as an option for treating active rheumatoid arthritis in adults whose disease has responded inadequately to, or who cannot tolerate, other disease-modifying antirheumatic drugs (DMARDs) including at least 1 tumour necrosis factor-alpha (TNF-alpha) inhibitor, only if:

- disease activity is severe and
- rituximab is contraindicated or not tolerated and
- the company provides certolizumab pegol with the agreed patient access scheme.

1.2 Certolizumab pegol, as monotherapy, is recommended as an option for treating active rheumatoid arthritis in adults whose disease has responded inadequately to, or who cannot tolerate, other DMARDs including at least 1 TNF-alpha inhibitor, only if:

- disease activity is severe and
- rituximab therapy cannot be given because methotrexate is contraindicated or not tolerated and
- the company provides certolizumab pegol with the agreed patient access scheme.

1.3 Continue treatment only if there is at least a moderate response measured using European League Against Rheumatism (EULAR) criteria at 6 months. After an initial response within 6 months, withdraw treatment if at least a moderate EULAR response is not maintained.

1.4 Take into account any physical, sensory or learning disabilities, or communication difficulties that could affect the responses to the disease activity score and make any appropriate adjustments.

1.5 This guidance is not intended to affect the position of patients whose treatment

with certolizumab pegol was started within the NHS before this guidance was published. Treatment of those patients may continue without change to whatever funding arrangements were in place for them before this guidance was published until they and their NHS clinician consider it appropriate to stop.

# 2 The technology

**Summary of certolizumab pegol**

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| **Description of the technology** | Certolizumab pegol (Cimzia, UCB Pharma) is a recombinant humanised antibody Fab' fragment against tumour necrosis factor-alpha (TNF-alpha) and is conjugated to polyethylene glycol (PEG). TNF-alpha is a pro-inflammatory mediator that is partly responsible for damage to the joints in rheumatoid arthritis. |
| **Marketing authorisation** | Certolizumab pegol in combination with methotrexate (MTX) has a marketing authorisation in the UK for 'the treatment of moderate to severe, active rheumatoid arthritis in adult patients when the response to disease-modifying antirheumatic drugs (DMARDs) including MTX, has been inadequate'. Certolizumab pegol can be given as 'monotherapy in case of intolerance to MTX or when continued treatment with MTX is inappropriate'.<br>Certolizumab pegol also has a marketing authorisation in combination with MTX for 'the treatment of severe, active and progressive rheumatoid arthritis in adults not previously treated with MTX or other DMARDs', but this is not within the remit of this technology appraisal. |
| **Adverse reactions** | Certolizumab pegol is contraindicated in people with active tuberculosis or other severe infections, and in people with moderate or severe heart failure. The summary of product characteristics lists no adverse reactions as very common but notes that in clinical trials the most common adverse reactions were bacterial and viral infections. For full details of adverse reactions and contraindications see the summary of product characteristics. |
| **Recommended dose and schedule** | The recommended starting dose of certolizumab pegol for adult patients is 400 mg (given as 2 subcutaneous injections of 200 mg each) at weeks 0, 2 and 4. After the starting dose, the recommended maintenance dose of certolizumab pegol is 200 mg every 2 weeks. Once clinical response is confirmed, an alternative maintenance dosing of 400 mg every 4 weeks can be considered. MTX should be continued during treatment with certolizumab pegol when appropriate. |

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| **Price** | The net price of certolizumab pegol is £357.50 per 200-mg prefilled syringe (excluding VAT; 'British national formulary' [BNF] edition 71). The company has agreed a patient access scheme with the Department of Health. In the scheme, the first 12 weeks of therapy (currently 10 pre-loaded syringes of 200 mg each) with certolizumab pegol are free of charge. The acquisition cost is £6,793 in the first year of treatment and then £9,295 per year. The Department of Health considered that this patient access scheme does not constitute an excessive administrative burden on the NHS. |

# 3 Evidence

The appraisal committee considered evidence submitted by UCB Pharma 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 certolizumab pegol, having considered evidence on the nature of rheumatoid arthritis and the value placed on the benefits of certolizumab pegol by people with the condition, those who represent them, and clinical experts. It also took into account the effective use of NHS resources.

## Clinical need and practice

4.1 The committee understood that the remit is to appraise certolizumab pegol when the response to other disease-modifying antirheumatic drugs (DMARDS), including a tumour necrosis factor-alpha (TNF-alpha) inhibitor, has been inadequate. It noted existing NICE guidance at this point in the treatment pathway (NICE technology appraisal guidance on adalimumab, etanercept, infliximab, rituximab and abatacept for rheumatoid arthritis, golimumab for rheumatoid arthritis and tocilizumab for rheumatoid arthritis). These recommend rituximab plus methotrexate after an inadequate response or intolerance to other DMARDs, including at least 1 TNF-alpha inhibitor. The committee was also aware that the guidance recommends adalimumab, etanercept, infliximab, abatacept, tocilizumab and golimumab (each with methotrexate) as options, when rituximab (plus methotrexate) is contraindicated or not tolerated and adalimumab and etanercept monotherapy as alternative options if rituximab therapy cannot be given because methotrexate is contraindicated or not tolerated. The committee heard from the patient experts that response to treatment is difficult to predict, because responses to biological DMARDs (bDMARDs) differ between people. The clinical expert emphasised the importance of a range of options for bDMARD treatments, particularly when rituximab plus methotrexate cannot be offered because of well-documented risks of adverse events occurring (for example, after infusion). The committee concluded that an additional treatment option for rheumatoid arthritis that has not responded to a TNF-alpha inhibitor would be valued by both patients and clinicians.

4.2 The committee was aware that the marketing authorisation covers the use of certolizumab pegol in moderate to severe disease. It was reminded that NICE

technology appraisal guidance on adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for rheumatoid arthritis not previously treated with DMARDs or after conventional DMARDs have failed recommends that treatment with a bDMARD should only be started when disease is severe, that is a disease activity (DAS28) score of more than 5.1. The committee understood that, at the point in the treatment pathway when treatment with the first bDMARD has not given an adequate response, severity of disease would have already been established. The committee was aware that there is a group of patients whose DAS28 score may be more than 5.1 when starting treatment with a first bDMARD, but whose DAS28 score may subsequently be less than 5.1 even though the disease has not adequately responded to the first bDMARD. The committee understood that this group would be small. It also understood from the consultation comments that this group would be considered to have severe disease, because the disease has already been confirmed as severe at an earlier point in the treatment pathway. The committee further noted that NICE technology appraisal guidance on adalimumab, etanercept, infliximab, rituximab and abatacept for rheumatoid arthritis and golimumab for rheumatoid arthritis do not define disease severity in the recommendations. Therefore, the committee did not consider it necessary to define disease severity using the DAS28 score measure when starting a second bDMARD.

# Decision problem

4.3 The committee considered the comparators for certolizumab pegol set out in the scope. It noted that the comparator was rituximab plus methotrexate. It was aware that, in line with existing NICE technology appraisal guidance (see section 4.1), alternative bDMARD treatment options were listed as comparators for those people for whom rituximab or methotrexate are contraindicated or withdrawn. The committee noted that the company had presented the evidence for 3 distinct populations, all of whom have been treated with a TNF-alpha inhibitor:

- people for whom rituximab is contraindicated or not tolerated
- people for whom methotrexate is contraindicated or not tolerated

- people for whom rituximab plus methotrexate is a treatment option.

4.4 The committee concluded that it was appropriate to consider the 3 groups as distinct from each other, and went on to consider the company's choice of comparators for each group. The committee noted that the company compared treatment sequences for the defined populations. The 3 tables below, show the sequences presented by the company. For the populations for whom methotrexate or rituximab is contraindicated, the sequences were of equal length and the comparator bDMARDs were:

- Abatacept, adalimumab, etanercept, golimumab, infliximab and tocilizumab (each plus methotrexate) when rituximab is contraindicated or not tolerated (table 1).
- Adalimumab monotherapy, etanercept monotherapy or tocilizumab monotherapy when rituximab therapy cannot be given because methotrexate is contraindicated or not tolerated (table 2).

**Table 1 Sequences for people for whom rituximab is contraindicated or not tolerated**

| Line of therapy | Sequence with certolizumab pegol (plus methotrexate) | Comparator sequence bDMARD (plus methotrexate) |
|---|---|---|
| 1st | Certolizumab pegol | Comparator biological |
| 2nd | Methotrexate plus hydroxychloroquine plus sulfasalazine | Methotrexate plus hydroxychloroquine plus sulfasalazine |
| 3rd | Leflunomide | Leflunomide |
| 4th | Gold injection | Gold injection |
| 5th | Ciclosporin | Ciclosporin |
| 6th | Azathioprine | Azathioprine |
| 7th | Palliative care | Palliative care |

**Table 2 Sequences for people for whom methotrexate is contraindicated or not tolerated**

| Line of therapy | Sequence with certolizumab pegol (monotherapy) | Comparator sequence bDMARD (monotherapy) |
|---|---|---|
| 1st | Certolizumab pegol | Comparator biological |
| 2nd | Leflunomide | Leflunomide |

| Line of therapy | Sequence with certolizumab pegol (monotherapy) | Comparator sequence bDMARD (monotherapy) |
|---|---|---|
| 3rd | Gold injection | Gold injection |
| 4th | Ciclosporin | Ciclosporin |
| 5th | Azathioprine | Azathioprine |
| 6th | Palliative care | Palliative care |

**Table 3 Sequences for people for whom rituximab is a treatment option**

| Line of therapy | Sequence with certolizumab pegol and bDMARDs (plus methotrexate) | Comparator sequence bDMARD (plus methotrexate) |
|---|---|---|
| 1st | Certolizumab pegol | Rituximab |
| 2nd | Rituximab | Tocilizumab |
| 3rd | Tocilizumab | Abatacept |
| 4th | Abatacept | Methotrexate plus hydroxychloroquine plus sulfasalazine |
| 5th | Methotrexate plus hydroxychloroquine plus sulfasalazine | Non-biological (weighted mix of leflunomide, gold, azathioprine and ciclosporin) |
| 6th | Non-biologic (weighted mix of leflunomide, gold, azathioprine and ciclosporin) | Palliative care |
| 7th | Palliative care | – |

The committee accepted the sequences for people for whom rituximab or methotrexate were contraindicated or not tolerated. It noted that for people for whom rituximab is a treatment option, the company compared treatment sequences of different lengths. The sequence containing certolizumab pegol placed certolizumab pegol before rituximab and therefore was not a strict comparison with rituximab because certolizumab pegol did not replace it, as with the other populations defined in the scope (see section 4.3). The committee considered that the sequences included treatments that would be offered to people whose disease has been classified as severe at the start of a first biological treatment. It recognised that the data provided by the company included people with moderate to severe disease, however the company did not separately compare treatment sequences for a population with moderate disease activity only. The committee therefore agreed it should focus on people with severe disease activity.

4.5 The committee heard evidence from the clinical expert on the use of biosimilar bDMARDs in clinical practice. It heard that infliximab biosimilars are not used in rheumatology and that the etanercept biosimilar has only been launched recently. It also heard that the etanercept biosimilar should be used in preference to its originator because it has lower acquisition costs. The committee concluded that, because the etanercept biosimilar is being used in clinical practice, it was appropriate to consider it in its decision-making.

# Clinical effectiveness

4.6 The committee considered the company's clinical evidence and accepted that the results showed that certolizumab pegol was more clinically effective than placebo. It understood that the only evidence available on the comparative effectiveness of certolizumab pegol and the bDMARDs was from the company's mixed treatment comparisons. The committee heard from the evidence review group (ERG) that there were problems with the methods used for these comparisons. In its response to consultation, the company acknowledged that there was heterogeneity between the studies and it provided a random-effects network meta-analysis to compare with its original fixed-effect network meta-analysis. The results from these analyses are academic in confidence and cannot be included here. The guide to the processes of technology appraisal states that in the interests of public transparency, data marked as confidential should be kept to an absolute minimum. Although it disagrees with the company assertion that including the analysis results would inhibit publication elsewhere, NICE considers it unreasonable to delay the appraisal and access for patients to negotiate further confidentiality lifting with the company, especially as the results were not fundamental to the committee's decision. In addition, while the point estimates from the network meta-analyses were marked as academic-in-confidence, the conclusions were presented publically and showed that the mean effect sizes from the random-effects model were equal to those of the fixed-effects model. The committee concluded that there are uncertainties in the estimates from the methods used and it could not reliably conclude whether certolizumab pegol was more clinically effective than the comparator bDMARDs on the basis of the mixed treatment comparisons presented by the company. The committee reasoned that certolizumab pegol has a similar mechanism of action to other TNF-alpha inhibitors, therefore it was plausible to assume that it would

have comparative efficacy to other bDMARDs. This reasoning was strengthened when the committee heard from the clinical expert that certolizumab pegol is already in use in clinical practice and is not considered to be better or worse than other TNF-alpha inhibitors. The committee concluded that certolizumab pegol has a similar efficacy to other available bDMARDs

# Cost effectiveness

4.7 The committee considered the cost-effectiveness evidence for the 3 populations defined in the company's submission (see section 4.1).

## People for whom rituximab or methotrexate are contraindicated or not tolerated

4.8 The committee was aware of its conclusion on the efficacy of certolizumab pegol and other bDMARDs (see section 4.6), It queried the base-case incremental cost-effective ratios (ICERs) in the company's submission for the populations of people for whom either rituximab or methotrexate are contraindicated or not tolerated. It would have expected to see similar quality-adjusted life year (QALY) gains to other bDMARDs, but the incremental QALY gain for certolizumab pegol plus methotrexate and certolizumab pegol as monotherapy, were 0.260 for both populations. The committee noted that the company stated there was a lack of comparative evidence in the population who have had TNF-alpha inhibitors before and therefore had to place assumptions on comparative effectiveness for the comparator bDMARDs. Therefore, the model assumed that the efficacy of adalimumab, etanercept and infliximab were equivalent to golimumab. The efficacies of adalimumab monotherapy and etanercept monotherapy were modelled using the effect size estimates for golimumab compared with certolizumab pegol (both in combination with methotrexate) from the network meta-analysis. The committee noted that these assumptions were not applied to certolizumab pegol.

4.9 The committee then considered the ERG's scenario analysis in which it assumed that certolizumab pegol had equal efficacy to etanercept, adalimumab and

infliximab (all plus methotrexate) for people for whom rituximab is contraindicated or not tolerated. The ERG also assumed that certolizumab pegol monotherapy had equal efficacy to etanercept and adalimumab monotherapies for people for whom methotrexate was contraindicated or not tolerated. The committee was aware that the etanercept biosimilar had been included in this sequence and agreed that this was appropriate. The committee noted for these equal length sequence analyses, that the ICERs for certolizumab pegol with methotrexate and as monotherapy were dominated; that is, certolizumab pegol plus methotrexate was more expensive but just as effective as the comparator bDMARDs. When the committee looked at the incremental increase in total costs between certolizumab pegol and the etanercept biosimilar it noted that there was very little difference so equivalence among the bDMARDs could be accepted. The committee considered the ICERs that incorporated confidential patient access schemes for abatacept and tocilizumab, the results of which cannot be shown here. Even when these schemes were taken into account, the committee noted that there were similarities in effects and costs and so concluded that certolizumab pegol plus methotrexate, or as monotherapy, can be considered a cost-effective use of NHS resources for people for whom rituximab or methotrexate are contraindicated or not tolerated.

## People for whom rituximab plus methotrexate is a treatment option

4.10 The committee had concerns about the company's approach to evaluating the cost effectiveness of certolizumab pegol plus methotrexate for this population. In particular, it was not persuaded that an intervention treatment sequence containing certolizumab pegol and 6 other treatments should be compared with the same sequence without certolizumab pegol (see section 4.4). The committee was aware from past technology appraisals that using different sequence lengths can increase modelling uncertainties. It heard from the ERG that the company's model may not be appropriate for comparing sequences of different lengths and this point was highlighted in the ERG's exploratory analysis in which the use of the same model type resulted in some counterintuitive results; the clinical benefit (shown by the QALY gain) appeared to be greater if a person had received rituximab plus methotrexate than if a person had received both certolizumab pegol plus methotrexate and rituximab plus methotrexate. In addition the

committee also understood that not all possible treatment sequences for this population had been included in the company's analysis. It noted that, to address this, the ERG had included 2 additional sequences in its exploratory analyses, in which certolizumab pegol plus methotrexate was placed after, and instead of, rituximab plus methotrexate. The committee noted that, after consultation, the company had accepted the relevance of the replacement sequence (that is, instead of rituximab plus methotrexate), but did not consider the sequence of certolizumab pegol after rituximab to be within the scope of the appraisal. The committee agreed with this but commented that placing certolizumab pegol plus methotrexate before rituximab plus methotrexate was also unsatisfactory (see section 4.4). It concluded that treatment sequences of the same length are preferable because they are subject to less uncertainty and that its focus should be on the sequence in which certolizumab pegol plus methotrexate replaces rituximab plus methotrexate.

4.11 In the revised base-case analysis submitted by the company after consultation, the committee understood that the company had accepted most of the ERG's preferred assumptions, except treatment duration for biological therapies, and the retreatment interval for rituximab. The committee noted that these were key drivers of cost effectiveness. It concluded that each of these should be examined before considering the ICERs for its preferred treatment sequence.

4.12 The company provided evidence from 2 studies to support an assumption of equal treatment duration for all biological therapies. A study by Ramiro et al. (2015) provided the evidence for a longer treatment duration with TNF-alpha inhibitors compared with non-TNF-alpha inhibitors, whereas a study by Du Pan et al. (2012) provided evidence for a shorter treatment duration with TNF-alpha inhibitors compared with non-TNF-alpha inhibitors. The committee was not persuaded that this opposing evidence should be interpreted as a basis for equal treatment duration. Also, it was not persuaded that these sources of evidence were methodologically stronger than the source preferred by the ERG (the REFLEX extension trial). In the Ramiro et al. (2015) trial, more people received a TNF-alpha inhibitor than a non-TNF-alpha inhibitor. Also, this study was done in the USA where prescription patterns, reimbursement decisions and patients' comorbidities differ from England. The committee had fewer concerns with the Du Pan et al. (2012) study because it had enrolled more comparable numbers of people on TNF-alpha and non-TNF-alpha inhibitors. Although the committee

acknowledged the company's concerns that trial conditions may not represent clinical practice, it regarded the evidence for rituximab, the comparator of interest, to be superior to that for a collection of non-TNF-alpha inhibitor technologies. The committee concluded that the data from the extension phase of the REFLEX trial provided the most appropriate source of evidence for treatment duration.

4.13 The committee considered the most plausible assumption for the retreatment interval of rituximab in the model. It noted that the summary of product characteristics for rituximab states that the 'need for further courses should be evaluated 24 weeks after the previous course', but did not consider that this was the same as specifying a 6-month retreatment interval. It also noted that the committee had previously discussed this assumption in NICE's technology appraisal guidance on adalimumab, etanercept, infliximab, rituximab and abatacept for rheumatoid arthritis, and concluded that treatment was unlikely to be as frequent as every 6 months for every person receiving rituximab. It therefore preferred the ERG's value of 10.09 months, which was sourced from the REFLEX trial. The committee considered that it was appropriate to use available trial evidence for rituximab to inform this assumption, and concluded that it was appropriate to use a retreatment interval for rituximab of 10.09 months.

4.14 In line with its conclusion about treatment sequences (see section 4.4), the committee considered the ICERs when certolizumab pegol plus methotrexate was placed in a sequence instead of rituximab plus methotrexate. The company's base-case estimate for this comparison was in excess of £130,000 per QALY gained. However, the committee recognised that its preferred assumptions for the treatment duration for bDMARDs and the rituximab retreatment interval were not incorporated in this estimate. When these preferred assumptions were included, certolizumab pegol plus methotrexate was dominated by rituximab plus methotrexate. This analysis did not take into account the confidential patient access scheme discount for tocilizumab, a treatment included in the treatment sequence after rituximab. When the confidential discount for tocilizumab was included, certolizumab pegol plus methotrexate was still dominated. In summary, the committee concluded that certolizumab pegol plus methotrexate could not be considered a cost-effective use of NHS resources when rituximab plus methotrexate is a treatment option. For completeness, the committee looked at the elongated sequence, in which certolizumab pegol plus methotrexate was

placed before rituximab plus methotrexate, which the committee had rejected earlier (see section 4.4 and section 4.10). The committee concluded that, with its preferred assumptions this sequence was still dominated and therefore was not a cost-effective use of NHS resources.

# Equality issues

4.15 The committee heard from the British Society of Rheumatology that certolizumab pegol may be used in pregnancy and that this was a potential equality issue. The committee was aware that the use of certolizumab pegol in pregnancy was outside the marketing authorisation. Because the committee makes recommendations within a technology's marketing authorisation, it could not consider including certolizumab pegol for use in pregnancy in its final recommendations. The committee concluded that it did not need to change its recommendations.

# Innovation

4.16 The company stated that not all the benefits of certolizumab pegol are captured by the QALY calculation, such as the effect the drug has on workplace and household productivity. However the committee considered that it had not been presented with any evidence to show an additional benefit over and above that already captured in the QALY. It concluded that all relevant benefits and costs were adequately captured by the QALY calculation.

# Pharmaceutical price regulations scheme (PPRS) 2014

4.17 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.

# 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 severe rheumatoid arthritis and the doctor responsible for their care thinks that certolizumab pegol is the right treatment, it should be available for use, in line with NICE's recommendations.

# 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 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.

**Hamish Lunagaria**
Technical Lead

**Joanne Holden**
Technical Adviser

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# Update information

**Minor changes since publication**

**June 2021:** Recommendation 1.4 added on equality when using the disease activity score.

ISBN: 978-1-4731-2127-0