

**NATIONAL INSTITUTE FOR HEALTH AND CARE
EXCELLENCE**

Final appraisal determination

**Baricitinib for moderate to severe rheumatoid
arthritis**

1 Recommendations

- 1.1 Baricitinib, with methotrexate, is recommended as an option for treating active rheumatoid arthritis in adults whose disease has responded inadequately to intensive therapy with conventional disease-modifying antirheumatic drugs (DMARDs), only if:
- disease is severe (a disease activity score [DAS28] of more than 5.1) and
 - the company provides baricitinib with the discount agreed in the patient access scheme.
- 1.2 Baricitinib, with methotrexate, is recommended as an option for treating active rheumatoid arthritis in adults whose disease has responded inadequately to or who cannot have other DMARDs, including at least 1 biological DMARD, only if:
- disease is severe (a DAS28 of more than 5.1) and
 - they cannot have rituximab and
 - the company provides baricitinib with the discount agreed in the patient access scheme.
- 1.3 Baricitinib can be used as monotherapy for people who cannot take methotrexate because it is contraindicated or because of intolerance, when the criteria in sections 1.1 and 1.2 are met.
- 1.4 Continue treatment only if there is a moderate response measured using European League Against Rheumatism (EULAR) criteria at 6 months after

starting therapy. After an initial response within 6 months, withdraw treatment if at least a moderate EULAR response is not maintained.

- 1.5 These recommendations are not intended to affect treatment with baricitinib that was started in the NHS before this guidance was published. Adults having treatment outside these recommendations 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

Clinical trials showed baricitinib plus conventional disease-modifying antirheumatic drugs (DMARDs) to be more effective than conventional DMARDs alone for treating severe active rheumatoid arthritis that has not responded adequately to conventional or biological DMARDs. Some trial evidence also suggests that in people who have not previously had DMARDs, baricitinib works as well when taken alone as it does when taken with conventional DMARDs.

Baricitinib plus conventional DMARDs was also shown to have similar effectiveness to the biological DMARD adalimumab in people whose disease has responded inadequately to conventional DMARDs. Because there are no trials which compare baricitinib with other biological DMARDs, the company did an indirect comparison. Baricitinib was shown to work as well as most of the biological DMARDs which NICE has already recommended in this indication.

Based on the health-related benefits and costs compared with conventional and biological DMARDs, baricitinib plus conventional DMARDs was recommended as a cost-effective treatment, in line with previous recommendations in NICE technology appraisal guidance on:

- [certolizumab pegol \(after a TNF-alpha inhibitor\)](#)

- [adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept \(after conventional DMARDs\)](#)
- [tocilizumab](#)
- [golimumab \(after DMARDs\)](#)
- [adalimumab, etanercept, infliximab, rituximab and abatacept \(after a TNF-alpha inhibitor\).](#)

2 The technology

Baricitinib (Olumiant, Eli Lilly)	
Marketing authorisation/anticipated marketing authorisation	Baricitinib has a marketing authorisation in the UK for the 'treatment of moderate to severe active rheumatoid arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying antirheumatic drugs.' Baricitinib can be given as monotherapy or in combination with methotrexate.
Recommended dose and schedule	The recommended dose of baricitinib is 4 mg once daily. A dose of 2 mg once daily is appropriate for patients aged 75 years and over and may be appropriate for patients with a history of chronic or recurrent infections. A dose of 2 mg once daily may also be considered for patients who have achieved sustained control of disease activity with 4 mg once daily and are eligible for dose-tapering.
Price	The list price of a 28-tablet pack of 2 mg or 4 mg baricitinib is £805.56. Each dose is also available in 84-tablet packs at a pro-rata price. The average cost per patient per year is estimated at £10,501 based on the list price. The company has agreed a patient access scheme with the Department of Health. This scheme provides a simple discount to the list price of baricitinib, with the discount applied at the point of purchase or invoice. The level of the discount is commercial in confidence. The Department of Health considered that this patient access scheme does not constitute an excessive administrative burden on the NHS.

3 Committee discussion

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

Treatment pathway

Baricitinib can be used at 4 different points in the pathway

- 3.1 Baricitinib's marketing authorisation covers its use at 4 points in the treatment pathway, specifically in adults with:
- moderate, active rheumatoid arthritis that has not responded adequately to conventional disease-modifying antirheumatic drugs (DMARDs)
 - severe, active rheumatoid arthritis that has not responded adequately to conventional DMARDs
 - severe, active rheumatoid arthritis that has not responded adequately to biological DMARDs, including at least 1 tumour necrosis factor-alpha (TNF-alpha) inhibitor
 - severe, active rheumatoid arthritis that has not responded adequately to biological DMARDs, including at least 1 TNF-alpha inhibitor and when rituximab is contraindicated or withdrawn because of adverse events.

The committee also noted that the marketing authorisation includes the use of baricitinib alone or with methotrexate.

NICE technology appraisal guidance exists for these points in the rheumatoid arthritis treatment pathway

- 3.2 NICE currently recommends the use of the biological DMARDs [adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept](#) (of which adalimumab, certolizumab pegol, etanercept, golimumab and infliximab are TNF-alpha inhibitors), in combination with methotrexate, in people with severe rheumatoid arthritis that has not responded to intensive treatment with combinations of conventional DMARDs. Disease severity is assessed using the disease activity score (DAS28). A DAS28 of more than 5.1 indicates severe disease (between 3.2 and 5.1 indicates moderate disease, less

than 3.2 but more than 2.6 indicates mild disease and less than 2.6 indicates disease remission). For people who meet these criteria but cannot take methotrexate, the guidance recommends that adalimumab, certolizumab pegol, etanercept or tocilizumab may be used as monotherapy.

- 3.3 For people with severe rheumatoid arthritis who have already had at least 1 TNF-alpha inhibitor that hasn't worked, NICE technology appraisal guidance on [adalimumab, etanercept, infliximab, rituximab and abatacept](#) recommends the biological DMARD rituximab in combination with methotrexate for treating severe active rheumatoid arthritis. If rituximab is contraindicated or withdrawn because of an adverse event, the guidance recommends abatacept, adalimumab, etanercept or infliximab in combination with methotrexate. If methotrexate is contraindicated or withdrawn because of an adverse event, the guidance recommends adalimumab or etanercept as monotherapy. NICE technology appraisal guidance on [tocilizumab](#) and [certolizumab pegol](#) recommend both treatments as alternatives to TNF-alpha inhibitors in the same circumstances (that is, for people with severe rheumatoid arthritis who have already had at least 1 TNF-alpha inhibitor that hasn't worked, in combination with methotrexate when rituximab is contraindicated or withdrawn and as monotherapy if methotrexate is contraindicated or withdrawn). NICE technology appraisal guidance also recommends [tocilizumab](#) in combination with methotrexate when neither TNF-alpha inhibitors nor rituximab have worked.

Baricitinib offers a new treatment option

- 3.4 The committee heard from the patient experts that rheumatoid arthritis is a lifetime condition that can severely reduce quality of life. The clinical experts stated that conventional DMARDs such as methotrexate are inadequate for many people. They added that the disease sometimes does not respond adequately to the first biological DMARD prescribed, and that there are few tools available to predict response to

help decide which treatment to use. Both the clinical and patient experts said it would be helpful to have new treatments that can be used at various points in the treatment pathway, alongside biological DMARDs after failure of conventional DMARDs. The clinical and patient experts agreed that methotrexate is often not well tolerated; the clinical experts noted that up to a third of people who are prescribed methotrexate with biological DMARDs do not take methotrexate because of side effects. The clinical experts emphasised that baricitinib is a novel treatment with a different mode of action to the biological DMARDs. They noted that the selective inhibition of Janus kinase 1 and 2 will affect a broad range of cytokines involved in the pathogenesis of rheumatoid arthritis. The clinical experts also noted the fast kinetic action of baricitinib compared with biological DMARDs. Both the clinical and patient experts also highlighted that baricitinib is given orally, which has major benefits for both patients and the health system. The patient experts emphasised that this is an important factor for people who have difficulty injecting themselves because of the disease affecting their hands. The patient experts also noted that some current treatments have to be stopped if the person gets an infection, and that some treatments may cause injection site reactions. The committee recognised that rheumatoid arthritis significantly affects quality of life. It concluded that there is a need for new treatment options, particularly when there is an inadequate response to conventional or biological DMARDs.

Subgroups

The company's subgroups and comparators were appropriate

3.5 The committee was aware that the company had analysed 4 distinct subgroups in which baricitinib could be used:

- People with moderate rheumatoid arthritis whose disease has responded inadequately to conventional DMARDs.
- People with severe rheumatoid arthritis whose disease has responded inadequately to conventional DMARDs.

- People with severe rheumatoid arthritis whose disease has responded inadequately to biological DMARDs and for whom rituximab is a treatment option.
- People with severe rheumatoid arthritis whose disease has responded inadequately to biological DMARDs and for whom rituximab is contraindicated or not tolerated.

The relevant comparators varied by subgroup. The committee concluded that it was appropriate to consider the 4 groups separately and that the company had broadly included the appropriate comparators.

Clinical effectiveness

The trials were adequate and suitable for decision-making

3.6 The company's clinical evidence came from 4 phase III randomised controlled trials and 1 long-term safety and tolerability study. The trials included people with moderate to severe rheumatoid arthritis, as defined in section 3.2. The trials were:

- RA-BEAM, which included people whose disease responded inadequately to methotrexate and who had not had biological DMARDs. Baricitinib 4 mg was given once daily and the comparators were placebo and adalimumab. Background methotrexate was given to all the groups.
- RA-BUILD, which included people whose disease responded inadequately to conventional DMARDs and who had not had biological DMARDs. Baricitinib 2 mg or 4 mg was given once daily and the comparator was placebo. People taking conventional DMARDs with or without methotrexate before the study continued to take background therapy.
- RA-BEACON, which included people whose disease responded inadequately to biological DMARDs. Baricitinib 2 mg or 4 mg was given once daily and the comparator was placebo. Background conventional DMARDs were given to all the groups.

- RA-BEGIN, which included people who had not had any conventional or biological DMARDs. Baricitinib 2 mg or 4 mg (both with methotrexate) was given once daily and the comparator was methotrexate. The committee was aware that the marketing authorisation for baricitinib does not include the treatment of rheumatoid arthritis in people who have not had any conventional or biological DMARDs (that is, this subgroup).

The long-term study safety and tolerability study, RA-BEYOND, included people with moderate or severe rheumatoid arthritis who were included in a separate phase IIb study or 1 of the 4 trials described above. Baricitinib 2 mg or 4 mg (both with methotrexate) was given only daily.

- 3.7 The primary outcome of all the randomised controlled trials was the proportion of people achieving a 20% improvement in the American College of Rheumatology response criteria (ACR20) at week 12 or 24. Secondary outcomes included the proportion of people achieving a 50% or 70% improvement in the response criteria (ACR50 and ACR70 respectively), and the proportion of people meeting the European League Against Rheumatism (EULAR) response criteria. The committee concluded that the trials were relevant and adequate for its decision-making.

Baricitinib is more clinically effective than conventional DMARDs alone and as effective as adalimumab for moderate to severe rheumatoid arthritis which has responded inadequately to conventional DMARDs

- 3.8 The committee considered RA-BEAM and RA-BUILD, which included people with moderate to severe rheumatoid arthritis which responded inadequately to conventional DMARDs. In RA-BEAM, there was a significant increase in the proportion of people meeting the ACR20 criteria at 12 weeks with 4 mg baricitinib plus conventional DMARDs compared with conventional DMARDs alone (odds ratio [OR] 3.6; 95% confidence interval [CI] 2.7 to 4.7, $p=0.001$). A smaller response was

seen with 4 mg baricitinib plus conventional DMARDs compared with adalimumab plus conventional DMARDs (OR 1.5; 95% CI 1.1 to 2.0, $p=0.014$ for ACR20). Significant improvements in ACR20 and EULAR good and moderate responses were also seen in RA-BUILD for 4 mg baricitinib plus conventional DMARDs compared with conventional DMARDs alone (OR 2.5; 95% CI 1.7 to 3.7, $p=0.001$ for ACR20 and OR 3.5; 95% CI 2.3 to 5.4, $p=0.001$ for EULAR). The committee also noted that in RA-BUILD, 2 mg baricitinib plus conventional DMARDs improved ACR20 and EULAR responses in this population compared with conventional DMARDs alone (OR 3.0; 95% CI 2.0 to 4.4, $p=0.001$ for ACR20 and OR 3.3; 95% CI 2.2 to 5.0, $p=0.001$ for EULAR good and moderate response). The committee concluded that 4 mg baricitinib plus conventional DMARDs has similar efficacy to adalimumab plus conventional DMARDs, and is more effective than conventional DMARDs alone in people with moderate to severe rheumatoid arthritis which has responded inadequately to conventional DMARDs.

Baricitinib is more clinically effective than conventional DMARDs alone for moderate to severe rheumatoid arthritis which has responded inadequately to biological DMARDs

- 3.9 The committee considered RA-BEACON, which included people with moderate to severe rheumatoid arthritis which responded inadequately to biological DMARDs. There was a significant increase in the proportion of people meeting the ACR20 criteria and having a EULAR moderate or good response rate at 12 weeks for 4 mg baricitinib plus conventional DMARDs compared with conventional DMARDs alone (OR 3.4; 95% CI 2.2 to 5.4, $p=0.001$ for ACR20 and OR 3.6; 95% CI 2.3 to 5.7, $p=0.001$ for EULAR moderate and good response). The committee also noted that 2 mg baricitinib plus conventional DMARDs also improved ACR20 and EULAR response rates in this population compared with conventional DMARDs alone (OR 2.7; 95% CI 1.7 to 4.2, $p=0.001$ for ACR20 OR 2.7; 95% CI 1.8 to 4.2, $p=0.001$ for EULAR moderate and good response). The committee concluded that both dosages of

baricitinib, when given with conventional DMARDs, are more effective than conventional DMARDs alone in people with moderate to severe rheumatoid arthritis which has responded inadequately to biological DMARDs.

Baricitinib has a similar safety profile to conventional DMARDs and adalimumab

3.10 The committee noted that across all 3 randomised controlled trials in which patients had previously had conventional or biological DMARDs (RA-BEAM, RA-BUILD and RA-BEACON), the safety profile of baricitinib was similar to that of the conventional DMARDs. In addition, it noted that the safety profiles were found to be similar in the head-to-head comparison of baricitinib and adalimumab (RA-BEAM).

Indirect comparison

Network meta-analyses show that baricitinib works as well as biological DMARDs

3.11 The committee was aware that other than the direct comparison with adalimumab, the only evidence available on the comparative effectiveness of baricitinib and the biological DMARDs was from the company's network meta-analyses. The company did separate analyses for patients whose disease inadequately responded to either conventional or biological DMARDs, using ACR and EULAR outcome measures.

At 24 weeks' follow-up, for patients whose disease inadequately responded to conventional DMARDs, the network meta-analysis showed:

- Baricitinib plus conventional DMARDs gave better EULAR response rates than conventional DMARDs alone.
- Baricitinib plus conventional DMARDs gave similar EULAR response rates to the biological DMARDs plus conventional DMARDs.

The exception to this was tocilizumab plus conventional DMARDs, which gave better EULAR result than all the other treatments. However, the clinical experts noted that the trials of tocilizumab had slightly different characteristics than the trials of the other technologies, and they considered tocilizumab to have similar effectiveness to the other biological DMARDs. Tocilizumab monotherapy showed similar results to baricitinib and the biological DMARDs when used with conventional DMARDs.

At 24 weeks' follow-up, for patients whose disease inadequately responded to biological DMARDs, the network meta-analysis showed:

- Baricitinib (2 mg and 4 mg) plus conventional DMARDs gave better EULAR response rates than conventional DMARDs alone. A dose response was seen, with 4 mg baricitinib having a better EULAR response than 2 mg baricitinib.
- Rituximab plus conventional DMARDs gave better EULAR response rates than baricitinib (2 mg and 4 mg) plus conventional DMARDs.

The company's and ERG's network meta-analysis results were broadly comparable

3.12 The committee heard from the ERG that there were problems with the methods used in the company's network meta-analysis. These included the conversion of ACR data to EULAR data before synthesis, the use of simultaneous models for baseline and treatment effects, the use of a random effects model for 1 population and a fixed effects model for the other, and poor model fit. In addition, the company had pooled the control data inappropriately. The ERG corrected the errors in the company's network meta-analysis. Having reviewed both analyses, the committee concluded that the results of the corrected network meta-analysis and the company's network meta-analysis (section 3.10) were broadly comparable.

Cost effectiveness

The cost-effectiveness studies presented by the company were appropriate

- 3.13 The company identified 9 UK-based cost-effectiveness studies. The committee was aware that 8 of these were associated with previous NICE technology appraisals guidance; 1 was an independent published review. The company did not identify any studies that included baricitinib, but the committee noted that the studies were nonetheless relevant and appropriate.

Economic model

The model structure was appropriate for decision-making

- 3.14 The company used an individual patient-based discrete event simulation model for its economic evaluation. The model simulates patients' disease progression through the sequences of treatments being compared. It was based on the model used by the assessment group during the production of NICE technology appraisal guidance on [adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for rheumatoid arthritis](#). The model categorised patients based on their EULAR response (good, moderate or no response) at 6 months. Response rates were based on the company's network meta-analysis. The company analysed cost effectiveness for each of the subgroups described in section 3.5. The committee concluded that the model structure was appropriate for its decision-making.

There were some concerns with how costs were calculated

- 3.15 The company's model included costs associated with drug acquisition, drug administration and monitoring, and hospitalisation. The committee was aware that baricitinib and several of the biological DMARDs have patient access schemes. It noted that the company had incorporated the patient access scheme prices for baricitinib, certolizumab pegol and

golimumab in the model, but not the confidential patient access schemes for abatacept and tocilizumab. The incremental cost-effectiveness ratios (ICERs) that incorporated these confidential patient access schemes cannot be reported here, however the range of ICERs usually considered to be cost effective is from £20,000 to £30,000 per quality-adjusted life year (QALY) gained. The company had also calculated the average cost of drug doses using the average weight, rather than the distribution of the weight of the modelled patient population. The committee was also aware that the company overestimated the number of doses and therefore the costs of infliximab.

The company is likely to have overestimated how well biological DMARDs work after an inadequate response to biological DMARDs and when rituximab is not an option

- 3.16 The company did not identify any evidence on the effectiveness of adalimumab, certolizumab pegol, etanercept or infliximab plus conventional DMARDs in patients with severe active rheumatoid arthritis which has responded inadequately to biological DMARDs when rituximab is contraindicated or not tolerated. In the absence of these data, the company used the same efficacy estimates for these treatments as those in patients with severe active rheumatoid arthritis which has responded inadequately to conventional DMARDs. The EULAR responses for all treatments were higher in these patients than in those with an inadequate response to biological DMARDs. The committee heard from the ERG that because of this, the company's base case is likely to have overestimated the efficacy of adalimumab, certolizumab pegol, etanercept and infliximab plus conventional DMARDs in patients with active rheumatoid arthritis which has responded inadequately to biological DMARDs when rituximab is contraindicated or not tolerated. The committee accepted this in the absence of any other evidence.

Utility values

The different approaches used to calculate utility were unlikely to change the overall conclusions

- 3.17 Health-related quality of life data were collected using EQ-5D-5L in RA-BEAM, RA-BUILD and RA-BEACON. Patient-level responses were converted to utility index-based health assessment questionnaire (HAQ) scores using the UK-specific scoring algorithm reported by Hernandez Alava et al. (2012). The committee was aware this was not in line with the analysis done during NICE's technology appraisal on [adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept](#), but it heard from the ERG that this approach was unlikely to change the overall conclusions.

The model was adequate for decision-making

- 3.18 The ERG identified several issues with the company's economic analyses including:
- Limitations with the company's network meta-analysis because an inappropriate random effects model was assumed for the baselines. In addition, simultaneous baseline and treatment effect models were used without ensuring that information in the baseline model did not propagate to the relative treatment effect model. Furthermore, studies that reported EULAR responses were synthesised along with converted EULAR response outcomes from studies that only reported ACR responses.
 - A lack of face validity in several of the scenario analyses, partly because of transcription and programming errors.
 - Limitations with the probabilistic sensitivity analyses because of programming errors, including an error which resulted in patients having some biological DMARDs never achieving a good or moderate EULAR response.

- Using the efficacy of treatments in the population with an inadequate response to conventional DMARDs for all biological DMARDs in the treatment sequence, regardless of their position in the sequence.
- Rounding HAQ scores to the nearest valid HAQ score, rather than allowing HAQ scores to be sampled based on a continuous HAQ value.
- Incorrect implementation of the HAQ trajectory classes by assigning each patient to a single class based on the probability of class membership, instead of using an average weighted by the probability of class membership.
- Assuming that patients who achieve a moderate or good EULAR response at 24 weeks had an instant reduction in HAQ score when starting treatment.
- Averaging HAQ across large time periods, which may lead to inaccurate results because the relationships between HAQ score and EQ-5D and between HAQ score and hospitalisation costs are not linear.
- Excluding intravenous abatacept and subcutaneous tocilizumab from the list of comparators, leading to inaccurate results.
- Using an older HAQ score to EQ-5D mapping than that used during the NICE appraisal of [adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept](#).
- Assuming that baricitinib would be used before intensive therapy with conventional DMARDs for patients with moderate rheumatoid arthritis (this was not supported by the clinical experts).
- Re-estimating the age of death at every event, which resulted in slightly different expected life years, which would be exacerbated by sequences of different lengths.
- Using the average weight of the population in the relevant trials to calculate average dose, which assumes there is a linear relationship between weight and dose costing and does not take into account drug wastage, for example.

- Overestimating the average number of doses, and thereby the cost, of infliximab that would be given in a year.

The ERG stated that these errors were unlikely to change the broad conclusions of the company's model. The committee concluded that although there were several errors in the company's economic model, it was adequate for its decision-making.

Baricitinib was comparable to other biological DMARDs in all of the company's scenario analyses

3.19 The company carried out several scenario analyses. In one, the company assumed that patients having conventional DMARDs or palliative care had a linear increase in their HAQ scores at a yearly rate of 0.045 and 0.060 respectively (based on Malottki et al. 2011), instead of using the latent class approach. For the moderate rheumatoid arthritis population, the ICER for baricitinib plus conventional DMARDs compared with intensive conventional DMARDs alone decreased from £37,420 to £20,965 per QALY gained. In the severe rheumatoid arthritis population, the ICERs were slightly lower for the most effective drugs. The committee heard from the ERG that the mapping used in Malottki et al. (2011) is not as robust as that used in Hernandez Alava et al. (2013). The company also:

- adjusted the HAQ score for baricitinib plus methotrexate so that it deteriorated at half of the rate assumed for conventional DMARDs
- used HAQ score improvements for baricitinib calculated from trial data rather than the UK rheumatoid arthritis database
- used a different time to treatment discontinuation for patients on baricitinib
- used alternative methods to map HAQ scores to the EQ-5D
- accounted for serious adverse events
- tapered baricitinib from 4 mg once daily to 2 mg once daily.

The committee heard from the ERG that these scenarios were unlikely to change the results of the cost-effectiveness analysis. The committee agreed that any exploratory analyses would not change its conclusion that baricitinib is broadly comparable to the other biological DMARDs recommended by NICE.

Cost-effectiveness results

Baricitinib is not cost effective for moderate disease after conventional DMARDs

3.20 In the moderate active rheumatoid arthritis population whose disease has responded inadequately to conventional DMARDs, the company's base-case ICER for the baricitinib sequence compared with the conventional DMARD sequence was £37,420 per QALY. The committee noted that the company used a different sequence for this population to that used in the NICE appraisal of [adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept](#). The ERG did not correct this or the errors in the model (see section 3.18) because they were unlikely to change the conclusions, and it could use the model from the other [appraisal](#) as a reference. The ERG noted that the median ICER of biological DMARDs in the NICE appraisal of [adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept](#) was around £50,000 per QALY gained. Taking into account the cost-effectiveness evidence for baricitinib in patients with moderate active rheumatoid arthritis whose disease has responded inadequately to conventional DMARDs, the committee considered that baricitinib plus conventional DMARDs did not have plausible potential to be cost effective in this population.

Baricitinib is cost effective for severe active rheumatoid arthritis after conventional DMARDs

3.21 In the company's base-case analysis for the severe rheumatoid arthritis population whose disease has responded inadequately to conventional

DMARDs, baricitinib plus conventional DMARDs dominated all its comparators (that is, it was both less costly and more effective). The exception to this was certolizumab pegol plus conventional DMARDs, which had an ICER of £18,400 per QALY compared with baricitinib plus conventional DMARDs. The committee noted that there are confidential patient access schemes in place for subcutaneous abatacept and intravenous tocilizumab, which the company did not include in its analysis. The ERG calculated new ICERs using the confidential comparator prices. The committee noted that all the comparisons produced very similar estimates of clinical and cost effectiveness, and concluded to recommend baricitinib plus conventional DMARDs as a cost-effective use of NHS resources for people with severe rheumatoid arthritis whose disease has responded inadequately to conventional DMARDs.

Baricitinib is not cost effective for severe disease after biological DMARDs if rituximab is a treatment option

3.22 In the company's base-case analysis for the severe rheumatoid arthritis population whose disease has responded inadequately to biological DMARDs and for whom rituximab is a treatment option, baricitinib plus conventional DMARDs was dominated by rituximab plus conventional DMARDs (that is, it was more costly and less effective). The committee concluded that baricitinib plus conventional DMARDs was not a cost-effective use of NHS resources for people with severe rheumatoid arthritis whose disease has responded inadequately to biological DMARDs if rituximab is a treatment option.

Baricitinib is cost effective for severe disease after biological DMARDs if rituximab is not a treatment option

3.23 In the pairwise analysis for the severe rheumatoid arthritis population whose disease has responded inadequately to biological DMARDs and for whom rituximab is contraindicated or not tolerated, baricitinib plus conventional DMARDs was dominated by golimumab plus conventional

DMARDs. Compared with all other comparators, the ICERs ranged from £16,201 to £484,782. In the full incremental analysis, baricitinib plus conventional DMARDs dominated or extendedly dominated all comparators except for certolizumab pegol plus conventional DMARDs, which had an ICER of £16,201 per QALY gained. The ICERs for biosimilar etanercept plus conventional DMARDs compared with baricitinib plus conventional DMARDs, and adalimumab plus conventional DMARDs compared with baricitinib plus conventional DMARDs, were also less than £30,000 per QALY gained. The committee again noted the confidential patient access schemes in place for subcutaneous abatacept and intravenous tocilizumab, which the company did not include in its analysis. The ERG calculated new ICERs using the confidential comparator prices. The committee noted that all the comparisons produced very similar estimates of clinical and cost effectiveness, and concluded to recommend baricitinib plus conventional DMARDs as a cost-effective use of NHS resources for people with severe rheumatoid arthritis whose disease has responded inadequately to biological DMARDs and for whom rituximab is not a treatment option.

The recommendations also apply to baricitinib monotherapy

- 3.24 The committee was aware that the marketing authorisation for baricitinib includes its use as a monotherapy, but that the company did not present an economic analysis for baricitinib alone for patients who cannot have methotrexate. The committee noted that the only available evidence for baricitinib alone is in people who have not had conventional DMARDs, which is outside of its marketing authorisation. The committee recognised the considerable uncertainty about the effectiveness of baricitinib alone in people whose rheumatoid arthritis has had an inadequate response to conventional or biological DMARDs. The committee heard from the ERG that data from RA-BEGIN showed that the addition of methotrexate to 4 mg baricitinib produced similar ACR scores compared with baricitinib alone. The committee agreed that baricitinib monotherapy provides similar clinical efficacy to baricitinib plus

conventional DMARDs. It concluded that its recommendations for baricitinib plus conventional DMARDs should also apply to baricitinib alone.

4 Implementation

- 4.1 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.
- 4.2 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.
- 4.3 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 baricitinib and the doctor responsible for their care thinks that baricitinib is the right treatment, it should be available for use, in line with NICE’s recommendations.
- 4.4 The Department of Health and Eli Lilly have agreed that baricitinib will be available to the NHS with a patient access scheme which makes it available with a discount. The size of the discount is commercial in confidence. It is the responsibility of the company to communicate details of the discount to the relevant NHS organisations. Any enquiries from NHS organisations about the patient access scheme should be directed to **[NICE to add details at time of publication]**.

5 Proposed date for review of guidance

- 5.1 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.

Andrew Stevens

Chair, appraisal committee C

May 2017

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.

Helen Powell

Technical lead

Final appraisal determination – Baricitinib for moderate to severe rheumatoid arthritis

Page 21 of 22

Issue date: June 2017

© National Institute for Health and Care Excellence 2017. All rights reserved.

Alexandra Filby

Technical adviser

Stephanie Yates

Project manager

ISBN: [to be added at publication]