NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Appraisal consultation document

Upadacitinib for treating moderate rheumatoid arthritis

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using upadacitinib for moderate rheumatoid arthritis 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?

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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 upadacitinib 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: 5pm on Friday 28 May 2021

Third appraisal committee meeting: TBC

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

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This guidance only includes recommendations for treating moderate rheumatoid arthritis.

The scope for this technology appraisal also included severe rheumatoid arthritis. This is covered by NICE technology appraisal guidance on upadacitinib for treating severe rheumatoid arthritis.

1 Recommendations

1.1 Upadacitinib with or without methotrexate is not recommended, within its marketing authorisation, for treating moderate active rheumatoid arthritis (a disease activity score [DAS28] of 3.2 to 5.1) in adults who cannot tolerate, or whose disease has responded inadequately to, 1 or more conventional disease-modifying antirheumatic drugs (DMARDs).

1.2 Take into account any physical, psychological, sensory or learning disabilities, or communication difficulties that could affect the responses to the DAS28 and make any appropriate adjustments.

1.3 These recommendations are not intended to affect treatment with upadacitinib that was started in the NHS before this guidance was published. People 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 trial evidence suggests that upadacitinib plus conventional DMARDs (including methotrexate) is more effective than placebo plus conventional DMARDs for treating moderate disease that has not responded well enough to conventional DMARDs. Evidence also suggests that upadacitinib alone is more effective than

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methotrexate for the same population. But the evidence may not reflect clinical practice, and it does not include people who could not tolerate methotrexate.

The cost-effectiveness results are uncertain. But they are likely to be higher than what NICE considers a cost-effective use of NHS resources. So upadacitinib, with or without methotrexate, is not recommended.

2 Information about upadacitinib

Marketing authorisation indication

2.1 Upadacitinib (Rinvoq, AbbVie) is indicated 'for the treatment of moderate to severe active rheumatoid arthritis in adult patients who have responded inadequately to, or who are intolerant to 1 or more disease-modifying antirheumatic drugs (DMARDs).' Upadacitinib may be used as monotherapy or in combination with methotrexate.

Dosage in the marketing authorisation

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

Price

2.3 The list price for upadacitinib is £805.56 per 28-day pack (company submission). The average cost for each patient per year is estimated at £10,508, based on the list price. The company has a commercial arrangement. This makes upadacitinib available to the NHS with a discount and it would have also applied to this indication if the technology had been recommended. 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 considered evidence submitted by AbbVie, a review of this submission by the evidence review group (ERG), NICE's technical report, and

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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. It agreed that the ERG's modelling of severe rheumatoid arthritis treatment sequences was acceptable for decision making. But it did not include all plausible sequences for people whose disease progressed from moderate to severe (see section 3.11).

After technical engagement, there were a number of outstanding uncertainties in the analyses (see technical report, pages 13 to 14). The committee took these into account in its decision making.

Treatments for rheumatoid arthritis

A range of treatment options is important in rheumatoid arthritis and upadacitinib is an additional option

3.1 The patient expert explained that rheumatoid arthritis is a lifetime condition that can severely reduce quality of life. The clinical experts stated that conventional disease-modifying antirheumatic drugs (DMARDs) such as methotrexate are inadequate for many people with active rheumatoid arthritis. Although a range of biological and targeted synthetic DMARDs are available for severe rheumatoid arthritis, only filgotinib is recommended for treating moderate disease (see NICE technology appraisal guidance on filgotinib for moderate to severe rheumatoid arthritis). But this was not recommended at the time of the committee's discussion, so it was not considered a comparator. Patient experts explained that currently people with moderate disease that has not responded adequately to conventional DMARDs have few effective treatment options. The committee concluded that it is important for people with moderate rheumatoid arthritis to have a range of treatment options.

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There are 2 different points in the moderate disease treatment pathway when upadacitinib might be used

3.2 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, between 2.6 and 3.2 indicates mild disease, and 2.6 or less indicates disease remission. Upadacitinib's marketing authorisation and the company's evidence submission covers its use at 2 points in the treatment pathway, specifically in adults with:

- Moderate disease that has not responded adequately to 1 conventional DMARD. The comparator at this position was conventional DMARDs.
- Moderate disease that has not responded adequately to 2 or more conventional DMARDs. At this position there were 2 potential comparators, conventional DMARDs or best supportive care (see section 3.3 and section 3.4).

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

The preferred position for upadacitinib is after 2 or more conventional DMARDs

3.3 The company presented results for upadacitinib at 2 positions in the moderate rheumatoid arthritis treatment pathway (see section 3.2). A clinical expert stated that it was more likely that upadacitinib would be used after 2 conventional DMARDs. Also, the European League Against Rheumatism (EULAR) guidelines state that 2 conventional DMARDs should be tried before considering a biological DMARD. But the guidelines recommend considering a biological DMARD after 1 conventional DMARD when poor prognostic factors are present. These include the presence of rheumatoid factor, antibodies against cyclic citrullinated peptide, high disease activity and early joint damage. The ERG explained that the company's network meta-analysis did not give separate results for people with a poor prognosis. Analyses done by the ERG showed that positioning

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upadacitinib after 1 conventional DMARD was likely to have a cost-effectiveness estimate much higher than £30,000 per quality-adjusted life year (QALY) gained, compared with positioning it after 2 or more conventional DMARDs. The committee concluded that the most appropriate position for upadacitinib was after treatment with 2 or more conventional DMARDs. It also concluded that, if methotrexate was tolerated, upadacitinib plus methotrexate was preferred to upadacitinib alone, based on the cost-effectiveness estimates. The committee noted that these conclusions were in line with previous NICE technology appraisals for rheumatoid arthritis.

The appropriate comparator after 2 conventional DMARDs is best supportive care, which is unlikely to give an EULAR response

3.4 In the company and ERG analysis, after 2 conventional DMARDs, there were 2 potential comparators: further conventional DMARD treatment or best supportive care. The clinical expert explained that at this position, further treatment with conventional DMARDs was not expected to give a response. Despite this, continued treatment was usually offered, and corticosteroids were also a treatment option. The company explained that best supportive care after 2 conventional DMARDs included some continued conventional DMARDs, particularly methotrexate. The committee concluded that after 2 conventional DMARDs, best supportive care is the conventional DMARDs that had been used before, with optional corticosteroids. This was the most appropriate comparator in this group because it reflects clinical practice. The committee also concluded that best supportive care is unlikely to give a response measured using EULAR criteria but noted this was difficult to account for (see sections 3.8 to 3.10).

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Clinical effectiveness

Subgroup analyses of the moderate population in SELECT-NEXT and SELECT-MONOTHERAPY trials are most relevant for decision making, but may not reflect clinical practice

3.5 The company's clinical evidence came from 4 phase 3 randomised controlled trials. The trials included people with moderate to severe rheumatoid arthritis (defined in section 3.2). The trials were:

- SELECT-COMPARE, which included people whose disease responded inadequately to methotrexate. Upadacitinib was taken with methotrexate and the comparator was adalimumab with methotrexate or placebo with methotrexate.
- SELECT-NEXT, which included people whose disease responded inadequately to at least 1 conventional DMARD. Upadacitinib was taken with conventional DMARDs and the comparator was placebo with conventional DMARDs.
- SELECT-MONOTHERAPY, which included people whose disease responded inadequately to methotrexate. Upadacitinib was taken as a monotherapy and the comparator was methotrexate.
- SELECT-BEYOND, which included people whose disease responded inadequately to biological DMARDs. Upadacitinib was taken with conventional DMARDs and the comparator was conventional DMARDs and placebo.

The committee considered the subgroup analyses of people with moderate disease. It noted that SELECT-NEXT was most relevant for the population who could tolerate methotrexate, because it included people who had an inadequate response to at least 1 conventional DMARD. It also included a higher proportion of people who were taking 2 conventional DMARDs at baseline, compared with SELECT-COMPARE (the exact data is confidential and cannot be reported here). The only trial that included a treatment effect for upadacitinib alone was SELECT-

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MONOTHERAPY. But it only included people who had had an inadequate response to methotrexate. The committee considered that it was reasonable to use the clinical-effectiveness data from this trial, even though it did not reflect the population of people who could not tolerate methotrexate. The committee concluded that SELECT-NEXT and SELECT-MONOTHERAPY were acceptable for decision making but may not reflect clinical practice.

Upadacitinib is more effective than conventional DMARDs for moderate disease

3.6 In the full population of SELECT-NEXT, upadacitinib with conventional DMARDs showed a statistically significant improvement in American College of Rheumatology response (ACR20) at 12 weeks, compared with placebo plus conventional DMARDs (upadacitinib 64%, placebo 36%, $p<0.001$). In SELECT-MONOTHERAPY, upadacitinib alone showed a statistically significant improvement in ACR20 at 12 weeks compared with methotrexate alone (upadacitinib 68%, methotrexate 41%, $p<0.001$). Similar results were seen for the moderate subgroups in both trials (exact data is confidential and cannot be reported here). The ERG and company considered that the safety profile for upadacitinib is similar to other biological DMARDs. The committee concluded that upadacitinib plus conventional DMARDs (including methotrexate) is more clinically effective than placebo plus conventional DMARDs (including methotrexate) for moderate disease. Also, it concluded that upadacitinib alone was more clinically effective than methotrexate alone for moderate rheumatoid arthritis that has responded inadequately to conventional DMARDs.

Direct head-to-head trial data is most appropriate to model efficacy of upadacitinib and best supportive care

3.7 A network meta-analysis was used for decision making for people with severe disease in NICE's technology appraisal of upadacitinib for treating severe rheumatoid arthritis. However, the ERG explained that for

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moderate disease, it may be more appropriate to use the SELECT trials because:

- the trials measured EULAR responses for all relevant comparators for moderate disease (with placebo plus conventional DMARDs used as a proxy for best supportive care, see section 3.9 and section 3.10)
- the company's method for estimating the placebo effect was uncertain and the ERG could not fully assess its reliability
- using direct head-to-head evidence is in line with NICE's guide to the methods of technology appraisal.

The committee concluded that direct head-to-head trial data were more appropriate to model efficacy of upadacitinib and best supportive care than the network meta-analysis results for moderate disease.

Modelling best supportive care

The company's revised analyses are not appropriate for decision making

3.8 The company submitted a revised base-case analysis after consultation and the first appraisal consultation document (ACD). This compared upadacitinib plus methotrexate with methotrexate alone, after 2 or more conventional DMARDs. In the comparator arm, the company used the treatment effect for methotrexate from its network meta-analysis for disease that had an inadequate response to conventional DMARDs. After methotrexate, the company modelled best supportive care. This was assumed to give no EULAR response (0% response rate). This was not in line with the committee's preferred assumptions, which were that best supportive care was the most appropriate comparator and that data from SELECT-NEXT and SELECT-MONOTHERAPY should be used to model the response rates. The committee concluded that the company's revised analyses were not appropriate for decision making.

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Analyses that adjust the response rates to account for response in the comparator arms are not appropriate

3.9 In response to technical engagement, the company provided a scenario analysis that estimated the 'net treatment effect' of upadacitinib compared with the trial control arms. This lowered the upadacitinib response rate to reflect that some of the response could be caused by a placebo or other effect. The company did not include the 'net treatment effect' in its revised base-case analysis. But it did provide scenario analyses that applied lower response rates to both the treatment and control arms, to reflect what would happen in clinical practice. The ERG explained that the methods used to reduce the response rate for upadacitinib may not be appropriate. This was because they:

- may have underestimated the treatment costs, because fewer people were assumed to have disease that responded to upadacitinib than would be expected. This lowered the costs of ongoing upadacitinib treatment
- may have biased the analysis for the costs of ongoing upadacitinib treatment, because a higher proportion of people were assumed to have a good EULAR response than may be expected in clinical practice
- cannot be applied to the trial data, which showed higher proportions of moderate EULAR responses in the comparator arms compared with the upadacitinib arm. This may not be expected in clinical practice.

The committee recognised that the company's scenario analyses were done to reflect clinical practice, but it raised the following methodological concerns:

- it is not known how much of the response in the comparator arm was caused by the placebo effect alone
- the analyses relied on trial data to adjust the EULAR response rates, categorised as 'good', 'moderate' or 'none'. But these were calculated

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from continuous DAS28 data. So, it is unlikely that the relative effects had been retained across the EULAR response categories

- there were no analyses using individual patient-level data to adjust the EULAR responses in the comparator arm, so it does not accurately reflect clinical practice.

In the absence of analyses based on patient-level adjusted data, the committee concluded that analyses that lower the trial response rates to account for the response rates in the comparator arm were not appropriate.

Using the placebo arms of the SELECT trials to model the efficacy of best supportive care has limitations but is acceptable

3.10 The ERG modelled the efficacy of best supportive care based on the response rates seen in the placebo plus conventional DMARDs arm of the SELECT-NEXT trial (the SELECT-MONOTHERAPY trial was used to model cost effectiveness for people who could not tolerate methotrexate see section 3.5). The committee recalled that best supportive care is not expected to give an EULAR response in clinical practice (see section 3.4). However, the committee noted that a considerable response rate was seen in the placebo arms of the SELECT trials, as well as in other clinical trials in rheumatoid arthritis. It noted that this response could have been caused by several factors, including a placebo effect, disease resolving naturally over time, regression to the mean, response bias and variation in symptoms. Some of these factors might have also contributed to the response to upadacitinib in the SELECT trials. Therefore, the committee agreed it would not be appropriate to assume full clinical efficacy for upadacitinib while assuming no response to best supportive care. The committee discussed whether it would be reasonable to assume that response rates decline at the same rate in placebo arms and treatment arms. If this were the case, there would be little difference in the relative treatment effect. When a EULAR response was completely lost, people would have best supportive care. But the ERG explained that people with

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a moderate response might be more likely to stop treatment than those with a good response. In the trials, a higher proportion of people had a moderate response in the comparator arm than the upadacitinib arm. The ERG's analyses also assumed that after this, all people had best supportive care with no efficacy until their disease progressed to severe. The committee preferred the ERG's analyses, which used SELECT-NEXT response rates for both upadacitinib with methotrexate and placebo plus conventional DMARDs (a proxy for best supportive care) because it retained the relative treatment effect seen in the clinical evidence. However, it acknowledged that these analyses had limitations because they did not fully reflect what is expected to happen in clinical practice.

Modelling progression from moderate to severe rheumatoid arthritis

Assuming 19% of people have disease progression after 2 years is appropriate but longer-term predictions may not reflect clinical practice

3.11 The company's model included treatment for moderate disease that had progressed to severe disease. This progression was not modelled in NICE's technology appraisal guidance on adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for rheumatoid arthritis (from now, TA375). However, the committee agreed that the progression reflects what happens in clinical practice. It noted that progression to severe disease had been modelled in NICE's technology appraisal of sarilumab for moderate to severe arthritis. This modelled progression by estimating the relationship between the DAS28 and health assessment questionnaire (HAQ) results from the clinical evidence. HAQ is 1 component of the ACR20 response criteria. It scores physical disability and pain from 0 (least disability) to 3 (most severe disability). The ERG noted that the company's original model did not apply this estimated relationship. In response to consultation and the first ACD, the company submitted 2 scenario analyses assuming that 11% and 19% of people with moderate disease have disease progression to severe

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disease after 2 years. The ERG explained that this was in line with the figure predicted by the UK Early Rheumatoid Arthritis Network database (19%). The committee noted that in the company's scenario analyses most people's disease progressed to severe after 12 years, which produced lower cost-effectiveness estimates for upadacitinib. The clinical expert estimated that in clinical practice around 30% of people with moderate disease were likely to have disease progression to severe disease by 12 years. The committee concluded that it was appropriate to assume that 19% of people with moderate disease have disease progression to severe disease after 2 years. But it further concluded that the company's longer-term predictions may be much lower in clinical practice.

Alternative treatment sequences after progression from moderate to severe disease are plausible

3.12 The committee understood that using upadacitinib to treat moderate disease could change the treatment pathway for severe disease. The ERG explored 3 alternative treatment sequences for severe disease: scenario 1, scenario 2 and a preferred scenario. These included people who can and cannot tolerate methotrexate. For people who can tolerate methotrexate, all treatments are taken in combination with methotrexate. Table 1 describes the treatment options in each scenario at first, second and third line for severe disease. The ERG's clinical expert explained that for people whose disease progresses to severe, adalimumab would generally be used first because it is the cheapest biological DMARD. If there was an inadequate response, rituximab is likely to be used next, even for people who cannot tolerate methotrexate. The ERG's clinical expert explained that in the first scenario analysis, people who have had upadacitinib could have abatacept instead of sarilumab because it works in a different way to upadacitinib. The ERG's second scenario explored using upadacitinib instead of sarilumab because people tend to prefer oral treatments to subcutaneous injections. The clinical expert agreed that abatacept, sarilumab and upadacitinib could be used as third-line

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treatment options. Fourth-line treatment is best supportive care in all the scenarios. The clinical expert clarified that the decision to use a particular treatment would depend on several factors including infection risk, liver function and cost of treatment. The committee understood that TA375 and the summary of product characteristics for rituximab recommend it is only used with methotrexate. It was concerned that the ERG's analyses may not reflect treatment sequences for people who cannot tolerate methotrexate, because rituximab is not licensed as a monotherapy. It understood that this was a small population and may reflect clinical practice but noted that treatment sequences may vary in the NHS in England. The committee concluded that the ERG's alternative treatment sequences for severe disease were plausible.

Table 1 Treatment sequences for people whose disease progresses from moderate to severe in the ERG's model

Scenario	Treatment arm	First-line treatment for severe disease	Second-line treatment for severe disease	Third-line treatment for severe disease
Preferred	Upadacitinib	Adalimumab	Rituximab	Sarilumab
Preferred	Best supportive care	Adalimumab	Rituximab	Sarilumab
Scenario 1	Upadacitinib	Adalimumab	Rituximab	Abatacept (subcutaneous)
Scenario 1	Best supportive care	Adalimumab	Rituximab	Sarilumab
Scenario 2	Upadacitinib	Adalimumab	Rituximab	Sarilumab
Scenario 2	Best supportive care	Adalimumab	Rituximab	Upadacitinib

Utility values

The company's and the ERG's mapping algorithms are plausible methods for estimating utility values

3.13 In the company's base-case analysis, health-related quality of life data were calculated using a mapping function to work out a person's pain

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score from their HAQ score. The mapping algorithm used data from the SELECT trials to estimate EQ-5D values. The ERG noted that TA375 used data from the National Databank for Rheumatic Diseases dataset to map pain scores from HAQ scores. It explained that the company's approach may be acceptable, but it preferred mapping based on the National Databank for Rheumatic Diseases dataset. This was because the dataset contained over 100,000 observations. After consultation and the first ACD, the company suggested that the mapping based on the National Databank for Rheumatic Diseases dataset produced some counterintuitive results. Some of the lowest functionality was associated with a reduction in pain. The company confirmed that this did not happen using its preferred method of mapping using data from the clinical trials. The committee noted that the choice of mapping did not have a large effect on cost-effectiveness estimates for severe disease, because health-related quality of life was similar across the different comparators. But it noted that for moderate disease, the company's method gave lower cost-effectiveness estimates for upadacitinib compared with best supportive care. The committee concluded that both mapping approaches were plausible, but noted that the ERG's approach was used in TA375 and was based on a much larger dataset.

The company's approach for modelling long-term health assessment questionnaire results is acceptable

3.14 In the ERG's preferred base-case analysis, people whose disease responded to best supportive care were assumed to have the same long-term HAQ results as those whose disease responded to biological DMARDs. The ERG explained that a large amount of the upadacitinib response was likely to have been caused by a placebo effect. This was also present in the trial control arms, so it may be inappropriate to make different assumptions about long-term HAQ results in the model. The clinical and patient experts advised that natural recovery from symptoms does not often happen, and it would not be sustained for a long time. The committee agreed that applying the long-term HAQ results associated

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with biological DMARDs to best supportive care was likely to be an overly optimistic assumption. In response to technical engagement, the company provided an alternative scenario analysis. In this, people whose disease responded to best supportive care were assumed to have the same long-term HAQ results as those whose disease responded to conventional DMARDs. The committee concluded that it was appropriate to assume that people whose disease responded to best supportive care had the same decreasing long-term HAQ results as people whose disease responded to conventional DMARDs. This was consistent with previous NICE technology appraisals in rheumatoid arthritis.

Economic model validation

The company's model is reasonably consistent with the model used in TA375

3.15 The company based its model on the model developed by the assessment group for TA375. The company provided a validation analysis comparing the outputs of its model with those from the model used in TA375, for several treatment sequences. The ERG suggested that the results of this analysis appeared to show that the company's model overestimated QALY gains for biological DMARDs compared with conventional DMARDs. It explained that this mostly affects the cost-effectiveness analysis for moderate disease, when upadacitinib is compared with conventional DMARDs. At the committee meeting, the company advised that it had found errors in the ERG's validation analysis and that its own model produced similar results to the TA375 model. After consultation and the first ACD, the company submitted further validation results that included corrections of 4 errors. The ERG noted that after consultation the company's results were reasonably aligned to TA375. The committee concluded that the company's model is reasonably consistent with the model used in TA375, which was considered acceptable for decision making.

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Cost-effectiveness results

Because of uncertainty in the cost-effectiveness estimates an acceptable ICER is £20,000 per QALY gained

3.16 NICE's guide to the methods of technology appraisal notes that above a most plausible incremental cost-effectiveness ratio (ICER) of £20,000 per QALY gained, judgements about the acceptability of a technology as an effective use of NHS resources will take into account the degree of certainty around the ICER. The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented.

The committee concluded that the cost-effectiveness results were uncertain because:

- the response rates in the placebo arms of the trials did not reflect clinical practice. It is unlikely that a EULAR response would be seen after an inadequate response with 2 conventional DMARDs (see section 3.9)
- the long-term rate of progression from moderate to severe disease is uncertain (see section 3.11)
- there is uncertainty about the most appropriate treatment sequence for people whose disease progresses from moderate to severe (see section 3.12).

Because of this uncertainty, the committee agreed that an acceptable ICER would be around £20,000 per QALY gained.

Upadacitinib with or without methotrexate is not cost-effective after 2 conventional DMARDs

3.17 The committee evaluated the cost effectiveness of upadacitinib for moderate disease based on the following conclusions:

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- the most appropriate position for upadacitinib in the moderate rheumatoid arthritis treatment pathway is after 2 conventional DMARDs (see section 3.3)
- best supportive care is the relevant comparator at this point in the treatment pathway (see section 3.4)
- subgroup analyses including only the moderate population from SELECT-NEXT and SELECT-MONOTHERAPY are appropriate to model the efficacy of both upadacitinib and best supportive care. After this, all people had best supportive care with no efficacy until their disease had progressed to severe (see section 3.5, section 3.7 and section 3.10)
- it is appropriate to assume 19% of people with moderate disease have disease progression to severe disease after 2 years, but longer-term predictions may not reflect clinical practice (see section 3.11)
- the ERG's alternative treatment sequences for severe disease were plausible but uncertain, particularly for the population who cannot tolerate methotrexate (see section 3.12)
- the company's and the ERG's mapping algorithms that link HAQ and pain scores are plausible methods for estimating utility values (see section 3.13)
- it is appropriate to assume that long-term HAQ results after response to best supportive care are different than after response to biological DMARDs (see section 3.14).

These scenarios included the confidential discounts for the comparators and subsequent treatments. They resulted in ICERs substantially higher than £20,000 per QALY gained, compared with best supportive care. The exact ICERs are confidential and cannot be reported here. The committee concluded that upadacitinib with or without methotrexate is not likely to be a cost-effective use of NHS resources for treating moderate disease, so did not recommend it.

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Other factors

Healthcare professionals should consider any disabilities or communication difficulties when using the DAS28 measure

3.18 During the scoping process a potential equality issue was raised about people with rheumatoid arthritis who have difficulty communicating. For these people, it may be more difficult to assess outcomes when using the DAS28 measure. The committee concluded that healthcare professionals should consider any physical, psychological, sensory or learning disabilities, or communication difficulties that could affect the responses to the DAS28 and make any appropriate adjustments.

The benefits of upadacitinib were captured in the cost-effectiveness analysis

3.19 Upadacitinib, like several other biological DMARDs, is taken orally. This is valued by patients. The committee noted that there are other oral treatments with a similar mechanism of action available for rheumatoid arthritis. It concluded that all the benefits of upadacitinib were captured in the model.

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.

Gary McVeigh
Chair, appraisal committee
November 2020

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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 D.

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.

Abitha Senthinathan and Alan Moore
Technical leads

Richard Diaz, Jamie Elvidge and Alex Filby
Technical advisers

Gavin Kenny and Gemma Barnacle
Project managers

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