NICE National Institute for Health and Care Excellence

NICE guidance

# Adalimumab, etanercept, infliximab and abatacept for treating moderate rheumatoid arthritis after conventional DMARDs have failed

Technology appraisal guidance
Published: 14 July 2021

www.nice.org.uk/guidance/ta715

# 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

This guidance should be read in conjunction with TA375.

# 1 Recommendations

1.1 Adalimumab, etanercept and infliximab, all with methotrexate, are recommended as options for treating active rheumatoid arthritis in adults, only if:

- intensive therapy with 2 or more conventional disease-modifying antirheumatic drugs (DMARDs) has not controlled the disease well enough and
- disease is moderate (a disease activity score [DAS28] of 3.2 to 5.1) and
- the companies provide adalimumab, etanercept and infliximab at the same or lower prices than those agreed with the Commercial Medicines Unit.

1.2 Adalimumab and etanercept can be used as monotherapy when methotrexate is contraindicated or not tolerated, when the criteria in 1.1 are met.

1.3 Continue treatment only if there is a moderate response measured using European League Against Rheumatism (EULAR) criteria at 6 months after starting therapy. If this initial response is not maintained, stop treatment.

1.4 If more than one treatment is suitable, start treatment with the least expensive drug (taking into account administration costs, dose needed and product price per dose). This may vary because of differences in how the drugs are used and treatment schedules.

1.5 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.

1.6 Abatacept with methotrexate is not recommended, within its marketing authorisation, for treating moderate active rheumatoid arthritis in adults when 1 or more DMARDs has not controlled the disease well enough.

**Why the committee made these recommendations**

This appraisal reviews some of the treatments (adalimumab, etanercept, infliximab and abatacept) recommended for severe rheumatoid arthritis in NICE technology appraisal guidance 375 and considers them for moderate rheumatoid arthritis. The clinical evidence suggests that these treatments are likely to be similarly effective in both moderate and severe disease.

The most likely estimates suggest that adalimumab, etanercept and infliximab after 2 or more conventional DMARDs are a cost-effective use of NHS resources. So, they are recommended for treating moderate rheumatoid arthritis. The most likely cost-effectiveness estimates for abatacept are higher than what NICE normally considers cost effective, so it is not recommended for moderate disease.

# 2 Information about adalimumab, etanercept, infliximab and abatacept

This technology appraisal includes 4 different biological medicines as either the originator medicine (the medicine first authorised for use) or a biosimilar product (see table 1). A biosimilar medicine is a medicine that is developed to be similar to an existing biological medicine.

**Table 1 Information about the technologies**

| Technology | Originator (company) | Biosimilar (company) | Mechanism of action | Method of administration |
|---|---|---|---|---|
| Adalimumab | Humira (AbbVie) | • Amgevita (Amgen)<br>• Imraldi (Biogen)<br>• Idacio (Fresenius Kabi)<br>• Hyrimoz (Sandoz) | Tumour necrosis factor (TNF)-alpha inhibitor | Subcutaneous injection |
| Etanercept | Enbrel (Pfizer) | • Benepali (Biogen)<br>• Erelzi (Sandoz) | TNF-alpha inhibitor | Subcutaneous injection |

| Technology | Originator (company) | Biosimilar (company) | Mechanism of action | Method of administration |
|---|---|---|---|---|
| Infliximab | – | • Flixabi (Biogen)<br>• Remsima (Celltrion Healthcare)<br>• Inflectra (Pfizer)<br>• Zessly (Sandoz) | TNF-alpha inhibitor | Intravenous injection |
| Abatacept | Orencia (Bristol-Myers Squibb) | – | Selective modulator of the T-lymphocyte activation pathway. Inhibits activation of T lymphocytes | Subcutaneous or intravenous injection |

The subcutaneous formulation of Remsima was not considered in this partial review because it was not included in the final scope for NICE technology appraisal guidance 375. The originator product for infliximab (Remicade) was also not considered because the manufacturer of this technology did not participate in this appraisal

# Adalimumab

2.1 Adalimumab (Humira, AbbVie; Amgevita, Amgen; Imraldi, Biogen; Idacio, Fresenius Kabi; Hyrimoz, Sandoz), in combination with methotrexate, is indicated 'for the treatment of moderate to severe, active rheumatoid arthritis in adult patients when the response to disease-modifying anti-rheumatic drugs including methotrexate has been inadequate'. Adalimumab can be given as monotherapy in case of intolerance to methotrexate or when continued treatment with methotrexate is inappropriate.

2.2 The dosage schedule is available in the summary of product

characteristics.

2.3 The list price of originator adalimumab (Humira, AbbVie) is £352.14 per 40 mg pre-filled pen or pre-filled syringe (excluding VAT; BNF online, accessed March 2021). The list price of adalimumab biosimilars per 40 mg pre-filled pen or pre-filled syringe are £316.80 (Amgevita, Amgen); £316.93 (Imraldi, Biogen); £316.93 (Idacio, Fresenius Kabi); £323.09 (Hyrimoz, Sandoz; all prices exclude VAT; BNF online, accessed March 2021).

2.4 The companies have each agreed a regional or nationally available price reduction for adalimumab with the Commercial Medicines Unit. The prices agreed through the framework are commercial in confidence.

# Etanercept

2.5 Etanercept (Enbrel, Pfizer; Benepali, Biogen; Erelzi, Sandoz) in combination with methotrexate, is indicated 'for the treatment of moderate to severe active rheumatoid arthritis in adults when the response to disease-modifying antirheumatic drugs, including methotrexate (unless contraindicated), has been inadequate'. Etanercept can be given as monotherapy in case of intolerance to methotrexate or when continued treatment with methotrexate is inappropriate.

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

2.7 The list price of originator etanercept (Enbrel, Pfizer) is £89.38 per 25 mg pre-filled pen or pre-filled syringe (excluding VAT; BNF online, accessed March 2021). The list price of etanercept biosimilars per 25 mg pre-filled pen or pre-filled syringe are £82.00 (Benepali, Biogen); £80.44 (Erelzi, Sandoz; all prices exclude VAT; BNF online, accessed March 2021).

2.8 The companies have each agreed a nationally available price reduction for etanercept with the Commercial Medicines Unit. The prices agreed through the framework are commercial in confidence.

# Infliximab

2.9 Infliximab (Flixabi, Biogen; Remsima, Celltrion Healthcare; Inflectra, Pfizer; Zessly, Sandoz), in combination with methotrexate, is indicated 'for the reduction of signs and symptoms as well as the improvement in physical function in: adult patients with active disease when the response to disease-modifying antirheumatic drugs (DMARDs), including methotrexate, has been inadequate'.

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

2.11 The list price of infliximab biosimilars per 100 mg vial are £377.00 (Flixabi, Biogen); £377.66 (Remsima, Celltrion Healthcare); £377.66 (Inflectra, Pfizer); £377.66 (Zessly, Sandoz; all prices exclude VAT; BNF online, accessed March 2021).

2.12 The companies have each agreed a nationally available price reduction for infliximab with the Commercial Medicines Unit. The prices agreed through the framework are commercial in confidence.

# Abatacept

2.13 Abatacept (Orencia, Bristol-Myers Squibb), in combination with methotrexate, is indicated for 'the treatment of moderate to severe active rheumatoid arthritis (RA) in adult patients who responded inadequately to previous therapy with one or more disease-modifying anti-rheumatic drugs (DMARDs) including methotrexate (MTX) or a tumour necrosis factor (TNF)-alpha inhibitor'.

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

2.15 The list price of abatacept (Orencia, Bristol-Myers Squibb) is £302.40 per 125 mg pre-filled pen or pre-filled syringe and £302.40 per 250 mg vial (excluding VAT; BNF online, accessed March 2021).

2.16 The company has a commercial arrangement. This makes abatacept

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 from a number of sources. See the committee papers for full details of the evidence.

This appraisal is a partial review of NICE technology appraisal guidance 375, which recommended adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept as treatment options for people with severe rheumatoid arthritis only, assessed by having a disease activity score (DAS28) more than 5.1. This partial review considers moderate disease, that is, with a DAS28 between 3.2 and 5.1. Although certolizumab pegol, golimumab and tocilizumab were included in the original guidance, the manufacturers of these technologies decided not to participate in this partial review. So, the committee could only consider adalimumab, etanercept, infliximab and abatacept when making recommendations for moderate disease.

A partial review has been done because biosimilar versions of adalimumab and etanercept are now available, and there have been changes in the prices for some of the other technologies. The committee assessed the cost effectiveness of the technologies using the original clinical evidence and economic model developed by the assessment group for NICE technology appraisal 375. The partial review has taken a pragmatic approach, which was consulted on in a review proposal, so the assessment group made only minor updates to the original model (see section 3.4 and section 3.5).

## New treatment options

### People with moderate rheumatoid arthritis would welcome new treatment options

3.1 The patient experts explained that people with moderate active rheumatoid arthritis have significant disability and reduced quality of life if their disease is not adequately controlled. This can affect a person's ability to work and do everyday activities. It also increases the need for continual NHS care. The patient experts described how this substantially affects emotional wellbeing, causing stress and anxiety, which can trigger further flare-ups of the disease. Although there are a range of

advanced treatment options for severe rheumatoid arthritis, only filgotinib is recommended for treating moderate disease after failure of 2 or more conventional disease-modifying antirheumatic drugs (DMARDs; such as methotrexate, leflunomide, sulfasalazine and hydroxychloroquine; see NICE's technology appraisal guidance on filgotinib). The committee noted that when this partial update started, the appraisal of filgotinib had not concluded. Therefore, filgotinib was not included in the scope as a comparator. The patient experts explained that it is important that there is a wide range of treatment options available for rheumatoid arthritis. This is because the differing nature of the disease means that a treatment may work well for one person but not another. The clinical experts explained that although the medicines appraised are similarly beneficial for treating the articular features of rheumatoid arthritis, they differ in their effectiveness in preventing particular comorbidities. This means that it is important for people with rheumatoid arthritis to have a range of different medicines available, even within the same drug class. The clinical experts explained that earlier access to advanced treatments in moderate disease would reduce disease progression and increase the likelihood of remission. The committee concluded that people with moderate rheumatoid arthritis would welcome a range of advanced treatment options.

# Cycling of TNF-alpha inhibitors

## This appraisal only considers first-line biological treatments in moderate disease

3.2 A company representative explained that the moderate treatment sequences modelled by the assessment group did not consider cycling of tumour necrosis factor (TNF)-alpha inhibitors (taking another TNF-alpha inhibitor after a first one). This would happen if a person does not tolerate the first treatment, or if their disease either does not respond or responds inadequately after an initial response. The clinical experts explained that because the technologies are protein-based drugs, there is a risk of developing antidrug antibodies, which reduces the treatment benefit over time. They noted that around 50% of people will stop treatment within 3 years because of loss of efficacy. The clinical experts

explained that the cycling of TNF-alpha inhibitors has a place in treating rheumatoid arthritis. They explained that, for this reason, having a variety of therapeutic choices for moderate disease would benefit people. The committee noted that the scope for the appraisal includes only first-line use of biological DMARDs (after a person's disease has responded inadequately to 2 or more conventional DMARDs) as in NICE technology appraisal guidance 375. It agreed that it was appropriate to assume that after the first biological treatment has failed, if the disease progresses to severe, NICE technology appraisal guidance for severe rheumatoid arthritis would be followed.

# Clinical evidence

## The clinical evidence used in NICE technology appraisal 375 is appropriate for this partial review

3.3 The clinical evidence used in this review is the same as that assessed in NICE technology appraisal guidance 375. So, the treatment efficacy of the interventions and comparators (adalimumab, etanercept, infliximab, abatacept all with methotrexate, and methotrexate alone) and subsequent treatments (rituximab and tocilizumab both with methotrexate) were informed by the results of the network meta-analysis done by the assessment group in NICE technology appraisal 375. The trials in the network meta-analysis included people with moderate and severe disease, so the efficacy of treatments was assumed to be the same in both populations. The committee considered the uncertainty around the midpoint estimates used when making its recommendations for treatments used in severe disease in NICE technology appraisal 375. The clinical experts explained that there is long-term clinical trial evidence and real-world evidence that strongly supports using biological DMARDs for treating moderate active disease. The committee concluded that the efficacy data accepted in the original guidance was appropriate to assess the cost effectiveness of adalimumab, etanercept, infliximab and abatacept for people with moderate active disease as part of this partial review.

# The assessment group's model

## The cost-effectiveness model used in NICE technology appraisal 375 is appropriate for this partial review

3.4 The assessment group developed an individual patient-based discrete event simulation model for its economic evaluation in NICE technology appraisal guidance 375. The scope for this appraisal included only the first-line use of biological DMARDs after an inadequate disease response to 2 or more conventional DMARDs. In the economic model, after the first biological treatment had failed, if disease progresses to severe, NICE technology appraisal guidance for severe rheumatoid arthritis was followed. For all analyses it was assumed that methotrexate was used in combination with the biological DMARD, and that the results for combination therapy could be generalised to biological DMARD monotherapy (if monotherapy use was included in the marketing authorisation). This assumption was also made in NICE technology appraisal 375. The model incorporated a response criterion based on European League Against Rheumatism (EULAR) response at 6 months to reflect UK clinical practice. If there was no EULAR response to a biological DMARD after 6 months then the next treatment in the strategy was used. Further details about the assessment group's original economic model can be found in the final guidance for NICE technology appraisal 375. The committee concluded that the cost-effectiveness model accepted in the original guidance was appropriate to use in this partial review, with some updates (see section 3.5).

## The changes to the assessment group's model are appropriate for decision making and reflect current NICE guidance

3.5 The assessment group's analyses included the assumptions preferred by the committee in NICE technology appraisal guidance 375. There were several updates to its original model:

- Updating the prices of interventions and subsequent treatments to reflect any changes to the prices of technologies.

- Amending the model so people with moderate disease who only have treatment with conventional DMARDs can have biological DMARDs after progression to severe disease (disease activity score [DAS28] more than 5.1). The committee understood that this treatment pathway was not an option in the original model but that it reflected current clinical practice. To include this change in the model, the assessment group estimated the relationship between changes in Health Assessment Questionnaire (HAQ) score, which was the measure used in the modelling, and changes in DAS28 score, which is the measure used to determine severity of disease. The assessment group did a systematic review to identify the best estimate of change in DAS28 score associated with a 0.125 change in HAQ score, which was considered to be 0.48. The assessment group also did sensitivity analyses using a lower estimate (the exact figure is confidential and cannot be reported here) and a higher estimate of 0.70.

- After stakeholder consultation, 1 company commented that the moderate treatment sequence used in the assessment group's updated model did not align with current NICE guidance recommendations for treating rheumatoid arthritis, or with the sequences modelled in NICE's technology appraisal guidance on filgotinib. In response, the assessment group further updated the treatment sequences used in the model to reflect current NICE guidance. The model assumed that for the treatment arm, a person with moderate disease would initially have a biological DMARD (either adalimumab, etanercept, infliximab or abatacept) followed by conventional DMARDs. For the comparator arm, the model assumed that a person would have initial treatment with methotrexate followed by other conventional DMARDs. Once disease progressed to severe (DAS28 more than 5.1) they would then move through a series of subsequent treatments.

## The treatment sequences in the updated economic model are appropriate

3.6 The trials included in the network meta-analysis showed people's disease responded to methotrexate (a conventional DMARD) when it is used as the first treatment. Therefore, the assessment group included a response to methotrexate when used as a first treatment in the comparator arm of the model (for people with moderate disease who had had 2 conventional DMARDs) but did not include a response to

methotrexate after a biological DMARD in the treatment arm of the model. The trials also showed a response with methotrexate following treatment with tocilizumab (in both treatment arms) and this efficacy was also included in the model in the treatment sequence for severe disease. The efficacy of conventional DMARDs when used later in the treatment pathway for moderate disease and at the end of the pathway in severe disease was assumed to be zero for both arms. In response to consultation, one consultee noted that in NICE technology appraisal guidance 375, in moderate disease, it was assumed that after biological treatments people would have methotrexate, which was associated with a response. A similar assumption was also made in NICE's technology appraisal guidance on baricitinib, tofacitinib and sarilumab. The committee noted that none of these appraisals had made positive recommendations for moderate disease. So, it did not consider that this point had been fully accepted by the committee in these appraisals. Also, it noted that it was debatable whether methotrexate would be used at this point in the treatment pathway or what size of response would be expected. However, because no new clinical evidence was being considered in this appraisal, it agreed there was no strong reason to deviate from the assumption put forward in NICE technology appraisal 375 and subsequent appraisals. The committee concluded that the assessment group's model was previously considered acceptable in NICE technology appraisal 375 and that the updates made to reflect current NICE guidance and consultation responses are appropriate for decision making (see table 2).

**Table 2 Treatment sequences used in the updated assessment group model**

| Treatment arm | Treatment | Comparator |
|---|---|---|
| **First treatment for moderate disease** | Biological DMARD | Methotrexate |
| **Second treatment for moderate disease** | Methotrexate | Conventional DMARDs |
| **Third treatment for moderate disease** | Conventional DMARDs | - |
| **First treatment for severe disease** | Adalimumab (infliximab if adalimumab is used in moderate disease) | Adalimumab |

| Treatment arm | Treatment | Comparator |
|---|---|---|
| **Second treatment for severe disease** | Rituximab | Rituximab |
| **Third treatment for severe disease** | Tocilizumab | Tocilizumab |

Abbreviations: DMARDs, disease-modifying antirheumatic drugs

# Cost-effectiveness estimates

## The most plausible ICERs for adalimumab, etanercept and infliximab are below £30,000 per QALY gained

3.7 NICE's guide to the methods of technology appraisal notes that above a most plausible incremental cost-effectiveness ratio (ICER) of £20,000 per quality-adjusted life year (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 agreed that an acceptable ICER would be within the range NICE normally considers a cost-effective use of NHS resources (£20,000 to £30,000 per QALY gained). Because of the confidential discounts for the treatments and some of the subsequent therapies, the exact ICERs are confidential and cannot be reported here. The assessment group's base-case analyses used the cheapest formulation of each intervention and prices included homecare support (when available). The assessment group's base-case ICERs for adalimumab and infliximab compared with conventional DMARDs were both substantially lower than £20,000 per QALY gained. The assessment group's base-case ICER for etanercept compared with conventional DMARDs was lower than £30,000 per QALY gained. For abatacept (intravenous and subcutaneous formulations) the ICER was substantially higher than £30,000 per QALY gained.

## The assessment group's sensitivity analyses do not change the

## cost-effectiveness conclusions

3.8 The assessment group did several sensitivity analyses including using lower (the exact figure is confidential and cannot be reported here) and higher values (0.70) for change in DAS28 score when HAQ score increases (see section 3.5). These had a small effect on the ICERs. Another sensitivity analysis was done to remove methotrexate after tocilizumab in the treatment sequences following progression to severe disease (in line with NICE's technology appraisal guidance on filgotinib), which also had little effect on the ICERs. The committee understood that there was some uncertainty about the efficacy estimates used in the model, which may have influenced the cost-effectiveness results. However, it agreed that these estimates were considered acceptable by the committee in NICE technology appraisal guidance 375. The committee discussed that there are multiple biosimilars for adalimumab, and the availability of these differs regionally in England, unlike etanercept and infliximab biosimilars, which are nationally available. The committee considered a further sensitivity analysis using the highest price that any region would need to pay for adalimumab. It was reassured that this did not change the cost-effectiveness conclusions for adalimumab.

## Adalimumab, etanercept and infliximab are cost-effective treatment options for moderate disease but abatacept is not recommended

3.9 The committee accepted the assessment group's updated base-case analyses. The assessment group's base-case ICERs for adalimumab and infliximab were both below the range NICE considers to be an acceptable use of NHS resources. Therefore, the committee recommended adalimumab and infliximab as first-line biological treatments for moderate active rheumatoid arthritis that has had an inadequate response to intensive therapy with 2 or more conventional DMARDs. Although the assessment group's ICER for etanercept was higher than those for adalimumab and infliximab, it was below £30,000 per QALY gained. In response to consultation, it was highlighted that there are some people for whom etanercept would be a particularly useful treatment option. For example, etanercept has a much lower risk of

reactivating latent tuberculosis, which has a higher prevalence in people with a South Asian family background. In addition, compared with some of the other biologicals, etanercept does not need to be stopped as far in advance by people wishing to conceive. The committee recognised that these groups would likely only represent a small number of people with moderate rheumatoid arthritis. The committee noted that the recommendations state that if more than 1 biological is an appropriate treatment option, treatment should start with the least expensive. So it also recommended etanercept as an option. The assessment group's base-case ICER for abatacept was above the range NICE considers to be an acceptable use of NHS resources. The committee therefore did not recommend abatacept as a treatment option for moderate active rheumatoid arthritis.

### Adalimumab monotherapy and etanercept monotherapy are also recommended for people who cannot have methotrexate

3.10 The committee agreed that people with moderate rheumatoid arthritis who cannot tolerate methotrexate should not be disadvantaged compared with other people with moderate disease, as far as possible. The committee concluded that, based on the marketing authorisation and the cost-effectiveness estimates, adalimumab and etanercept could be recommended as monotherapy for moderate active disease previously treated with conventional DMARDs.

## Equality considerations

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

3.11 A potential equality issue was raised in NICE's technology appraisal guidance on upadacitinib for treating severe rheumatoid arthritis, 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 agreed that this equality issue was also important to consider for this appraisal. 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.

## Etanercept may be particularly beneficial for some people with protected characteristics

3.12 Some of the people for whom etanercept may be particularly beneficial have protected characteristics. The committee took this into account in its decision making about etanercept (see section 3.9).

## No other equality issues have been identified that can be addressed in this technology appraisal

3.13 The patient experts explained that certolizumab pegol, another TNF-alpha inhibitor, is often used to treat rheumatoid arthritis in women who are planning to become pregnant or who are pregnant. They described how not having this as a treatment option for people with moderate disease could potentially discriminate against women of childbearing age. The clinical experts explained that certolizumab pegol does not easily cross the placenta so is usually the preferred treatment choice during pregnancy. However, they explained that other TNF-alpha inhibitors can be used in different stages of pregnancy but that there is a risk of active transport across the placenta, which often means that treatment is stopped. The committee concluded that this issue could not be addressed in this technology appraisal, because the company manufacturing certolizumab pegol decided not to participate in this partial review. So, the committee could not make recommendations on its use for moderate disease.

# Other factors

## Healthcare professionals should choose the most appropriate treatment after discussing the options with the person having treatment

3.14 The committee understood that having a range of treatment options is important in treating moderate rheumatoid arthritis. It understood that NICE recommended filgotinib for treating moderate to severe rheumatoid arthritis (see NICE's technology appraisal guidance on filgotinib) and noted NICE's ongoing technology appraisal on upadacitinib for previously treated moderate active rheumatoid arthritis. The committee concluded that healthcare professionals should choose the most appropriate treatment after discussing the advantages and disadvantages of the treatments available with the person having treatment. If more than 1 treatment is suitable, they should start treatment with the least expensive drug (taking into account administration costs, dose needed and product price per dose). This may vary because of differences in how the drugs are used and treatment schedules.

## The benefits of the technologies were adequately captured in the cost-effectiveness analysis

3.15 The patient and clinical experts explained that biological DMARDs are highly effective in reducing disease progression and improving quality of life in people with rheumatoid arthritis. The committee noted that biological DMARDs were considered to be innovative in NICE technology appraisal guidance 375 for people with severe disease. It discussed that while filgotinib is the only advanced treatment option currently available for people with moderate disease, its mechanism of action is different to the biological DMARDs, of which none are currently available for people with moderate disease. The committee agreed that the technologies are important treatment options for these people. It concluded that all the benefits of the technologies were adequately captured in the model.

# 4 Implementation

4.1 Section 7 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 ministers have 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 2 months of the first publication of the final appraisal document.

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 moderate active rheumatoid arthritis and the doctor responsible for their care thinks that adalimumab, etanercept or infliximab are the right treatment, it should be available for use, in line with NICE's recommendations.

# 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 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.

**Anita Sangha**
Technical lead

**Alexandra Filby**
Technical adviser

**Louise Jafferally**
Project manager

# Update information

**August 2021:** Recommendation 1.3 updated to clarify when to stop treatment.

ISBN: 978-1-4731-4179-7