

Sarilumab for moderate to severe rheumatoid arthritis

Technology appraisal guidance

Published: 1 November 2017

www.nice.org.uk/guidance/ta485

Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

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

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should [assess and reduce the environmental impact of implementing NICE recommendations](#) wherever possible.

Contents

1 Recommendations	4
2 The technology.....	7
3 Committee discussion	8
Treatment pathway	8
Subgroups.....	10
Clinical effectiveness.....	11
Indirect comparison	14
Cost effectiveness	16
Cost-effectiveness results	19
4 Implementation.....	23
5 Appraisal committee members and NICE project team	24
Appraisal committee members	24
NICE project team	24
Update information	25

1 Recommendations

- 1.1 Sarilumab, with methotrexate, is recommended as an option for treating active rheumatoid arthritis in adults whose disease has responded inadequately to intensive therapy with a combination of 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 sarilumab with the discount agreed in the patient access scheme.
- 1.2 Sarilumab, 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 sarilumab with the discount agreed in the patient access scheme.
- 1.3 Sarilumab, with methotrexate, is recommended as an option for treating active rheumatoid arthritis in adults whose disease has responded inadequately to rituximab and at least 1 biological DMARD, only if:
- disease is severe (a DAS28 of more than 5.1) and
 - the company provides sarilumab with the discount agreed in the patient access scheme.
- 1.4 Sarilumab 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 or 1.2 are met.
- 1.5 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.

- 1.6 When using the DAS28, healthcare professionals should take into account any physical, psychological, sensory or learning disabilities, or communication difficulties that could affect the responses to the DAS28 and make any adjustments they consider appropriate.
- 1.7 These recommendations are not intended to affect treatment with sarilumab 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 trials showed sarilumab plus methotrexate or conventional DMARDs to be more effective than methotrexate or conventional DMARDs for treating moderate to severe active rheumatoid arthritis that has not responded adequately to conventional DMARDs. The trials also showed that for treating severe active rheumatoid arthritis that has not responded adequately to conventional DMARDs, sarilumab alone is more effective than adalimumab alone.

Because there are no trials comparing sarilumab with other biological DMARDs, the company did an indirect comparison. This showed that sarilumab with conventional DMARDs (including methotrexate) or alone works as well as most of the biological DMARDs that NICE has already recommended.

Based on the health-related benefits and costs compared with conventional and biological DMARDs, sarilumab plus methotrexate or sarilumab alone is recommended as a cost-effective treatment for severe active rheumatoid arthritis, in line with previous recommendations in:

- [NICE technology appraisal guidance on baricitinib](#)
- [certolizumab pegol \(after a TNF-alpha inhibitor\)](#)

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

2 The technology

Information about sarilumab

Marketing authorisation	Sarilumab (Kevzara, Sanofi) has a marketing authorisation in the UK for the 'treatment of moderately to severely active rheumatoid arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying antirheumatic drugs.' Sarilumab can be given as monotherapy or in combination with methotrexate.
Recommended dose and schedule	The recommended dose of sarilumab is 200 mg administered once every 2 weeks. A reduction in dose from 200 mg once every 2 weeks to 150 mg once every 2 weeks is recommended for management of neutropenia, thrombocytopenia and liver enzyme elevations. Sarilumab is administered subcutaneously using a pre-filled pen or syringe. See the summary of product characteristics for details.
Price	<p>The list price per pre-filled pen or syringe of 150 mg or 200 mg of sarilumab is £456.13.</p> <p>The average cost per patient per year is estimated at £11,900 based on the list price.</p> <p>The company has agreed a patient access scheme with the Department of Health. This scheme provides a simple discount to the list price of sarilumab, 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.</p>

3 Committee discussion

The appraisal committee ([section 5](#)) considered evidence submitted by Sanofi and a review of this submission by the evidence review group (ERG). See the [committee papers](#) for full details of the evidence.

Treatment pathway

Sarilumab can be used at 5 different points in the pathway

- 3.1 Sarilumab's marketing authorisation and the company submission covers its use at 5 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
 - severe, active rheumatoid arthritis that has not responded adequately to biological DMARDs, when rituximab is contraindicated or withdrawn because of adverse events
 - severe, active rheumatoid arthritis that has not responded adequately to rituximab and biological DMARDs.

The committee also noted that the marketing authorisation includes the use of sarilumab 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 in its [technology appraisal guidance on baricitinib](#), and [adalimumab](#),

etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept (of which adalimumab, certolizumab pegol, etanercept, golimumab and infliximab are tumour necrosis factor (TNF)-alpha inhibitors) and tofacitinib, 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 2.6 or less indicates disease remission). For people who meet these criteria but cannot take methotrexate, the guidance recommends that adalimumab, baricitinib, certolizumab pegol, etanercept or tocilizumab may be used as monotherapy. The guidance recommends treatment should start with the least expensive drug (taking into account administration costs, dose needed and product price per dose) and should only be continued according to EULAR response at 6 months.

- 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 and golimumab recommend the biological DMARD rituximab in combination with methotrexate for treating severe active rheumatoid arthritis. But, if rituximab is contraindicated or withdrawn because of an adverse event, NICE technology appraisal guidance recommends abatacept, adalimumab, etanercept, infliximab, golimumab, tocilizumab, certolizumab pegol, baricitinib or tofacitinib in combination with methotrexate. If methotrexate is contraindicated or withdrawn because of an adverse event, NICE's guidance recommends adalimumab, etanercept, certolizumab pegol, baricitinib or tofacitinib as monotherapy. NICE technology appraisal guidance also recommends tocilizumab in combination with methotrexate when neither TNF-alpha inhibitors nor rituximab have worked. See the [NICE Pathway on rheumatoid arthritis](#) for more details.

Sarilumab offers an additional treatment option

- 3.4 The patient experts explained that rheumatoid arthritis is a lifetime condition that can severely reduce quality of life. The clinical expert

stated that choosing an appropriate treatment depends on disease severity and response to treatment. The clinical expert noted that the disease sometimes does not respond adequately to the first biological DMARD prescribed. When there is not an adequate response the treatment is stopped and the next available treatment in the pathway is prescribed. 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 highlighted that sarilumab is administered by injection at home, which has major benefits for both patients and the health system. Sarilumab has a longer shelf-life when kept out of the fridge and the clinical expert emphasised that having a treatment that lasts 14 days rather than a number of hours is an important practical factor for people, especially those who travel. 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 are appropriate

3.5 The company analysed 5 distinct subgroups in which sarilumab could be used. These were people with:

- moderate, active rheumatoid arthritis that has not responded adequately to conventional 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 TNF-alpha inhibitor
- severe, active rheumatoid arthritis that has not responded adequately to biological DMARDs, when rituximab is contraindicated or withdrawn because of adverse events

- severe, active rheumatoid arthritis that has not responded adequately to rituximab and biological DMARDs.

The relevant comparators varied by subgroup. The committee concluded that it was appropriate to consider the 5 groups separately and that the company had included the appropriate comparators.

Clinical effectiveness

The trials are adequate and suitable for decision-making

3.6 The company's clinical evidence came from 5 randomised controlled trials and 1 long-term safety study. The trials included people with moderate to severe rheumatoid arthritis, as defined in section 3.2. The trials were:

- MOBILITY-A, a phase II trial which included people whose disease responded inadequately to methotrexate. Five sarilumab doses (100 mg or 150 mg once weekly and 100 mg, 150 mg or 200 mg once every 2 weeks) were given in combination with methotrexate and the comparator was methotrexate plus placebo. The primary outcome was the proportion of people who had a 20% improvement in the American College of Rheumatology response criteria (ACR20) at week 12.
- MOBILITY-B, a phase III trial which included people whose disease responded inadequately to methotrexate. Sarilumab 150 mg or 200 mg was given once every 2 weeks in combination with methotrexate and the comparator was methotrexate plus placebo. The primary outcomes were: the proportion of people reaching ACR20 at week 24; change in physical function using the Health Assessment Questionnaire Disability Index (HAQ-DI) at week 16; and the change in Modified Total Sharp Score (mTSS) at week 52.
- MONARCH, a phase III trial which included people whose disease responded inadequately or who were intolerant to methotrexate. Sarilumab 200 mg plus placebo was given once every 2 weeks and the comparator was adalimumab plus placebo. The primary outcome was the change from baseline in disease activity score 28 – erythrocyte sedimentation rate (DAS28-ESR) at week 24.

- TARGET, a phase III trial which included people whose disease responded inadequately or who were intolerant to TNF-alpha inhibitors. Sarilumab 150 mg or 200 mg was given once every 2 weeks in combination with conventional DMARDs. The comparator was placebo plus conventional DMARDs. The primary outcomes were the proportion of people reaching ACR20 at week 24 and the change in physical function using HAQ-DI at week 12.
- ASCERTAIN, a phase III trial which included people whose disease responded inadequately or who were intolerant to TNF-alpha inhibitors. Sarilumab 150 mg or 200 mg was given once every 2 weeks in combination with conventional DMARDs. The comparator was tocilizumab 4 to 8 mg plus conventional DMARDs. The primary outcome was description and number of adverse events.
- EXTEND, a phase III open-label extension study which included people whose disease responded inadequately to methotrexate and TNF-alpha inhibitors. The trial assessed sarilumab plus conventional DMARDs and sarilumab monotherapy. The primary endpoint was safety.

The committee concluded that the trials were relevant and adequate for its decision-making.

Sarilumab plus methotrexate is more clinically effective than placebo plus methotrexate, and sarilumab alone is more clinically effective than adalimumab alone for moderate to severe rheumatoid arthritis which has responded inadequately to conventional DMARDs

- 3.7 In MOBILITY-A, sarilumab plus methotrexate showed a statistically significant improvement in ACR20 at 12 weeks compared with placebo plus methotrexate (sarilumab 200 mg 65%, placebo 46%; $p=0.0426$). In MOBILITY-B, sarilumab plus methotrexate showed a statistically significant improvement in ACR20 at 24 weeks compared with placebo plus methotrexate (sarilumab 200 mg 66%, placebo 33%; $p<0.0001$). In MONARCH, sarilumab plus placebo showed a statistically significant improvement in ACR20 at 24 weeks compared with adalimumab 40 mg plus placebo (sarilumab 200 mg 72%, adalimumab 40 mg 58%;

p=0.0074). The committee concluded that sarilumab plus methotrexate is more clinically effective than placebo plus methotrexate, and that sarilumab alone is more clinically effective than adalimumab alone for moderate to severe rheumatoid arthritis which has responded inadequately to conventional DMARDs.

Sarilumab is more clinically effective than conventional DMARDs for moderate to severe rheumatoid arthritis which has responded inadequately to TNF-alpha inhibitors

3.8 The TARGET trial showed that sarilumab plus methotrexate led to a statistically significant improvement in ACR20 compared with methotrexate at 24 weeks (sarilumab 200 mg 61%, placebo 34%; p<0.001). The company did not report comparative statistics for ASCERTAIN because the trial was powered for safety rather clinical effectiveness. The committee concluded that sarilumab is more clinically effective than conventional DMARDs for moderate to severe rheumatoid arthritis which has responded inadequately to TNF-alpha inhibitors.

Sarilumab has an increased rate of adverse events compared with methotrexate

3.9 In the MOBILITY trials the rate of adverse events was higher in the sarilumab 200 mg group (ranging from 65% to 78%) compared with the methotrexate group (ranging from 47% to 62%). In the MONARCH trial, adalimumab and sarilumab had similar adverse event rates (63.6% and 64.1% respectively). The committee concluded that sarilumab plus methotrexate has a slightly higher rate of adverse events compared with methotrexate.

Indirect comparison

Network meta-analyses show that sarilumab with conventional DMARDs or alone works as well as biological DMARDs

3.10 Because the only direct evidence available on the comparative effectiveness of sarilumab and the biological DMARDs was with adalimumab, the company did a network meta-analyses. The company did separate analyses for patients whose disease responded inadequately to either conventional or biological DMARDs, using ACR20/50/70 score, HAQ-DI, European League Against Rheumatism (EULAR) responses, DAS28 remission, mTSS, serious infections and serious adverse events. In the conventional DMARD group the analyses were further split into combination therapy and monotherapy. EULAR responses were not identified for all the relevant comparators in the NICE scope because of a lack of reporting in the trials. The company transformed ACR responses into EULAR responses to inform treatment effectiveness in the economic model ([section 3.13](#)). At 24 weeks' follow-up, for patients whose disease responded inadequately to conventional DMARDs, the network meta-analysis showed:

- sarilumab 200 mg plus conventional DMARDs gave better ACR20/50/70 response rates than conventional DMARDs
- sarilumab 200 mg plus conventional DMARDs gave similar ACR20/50/70 response rates to the biological DMARDs
- sarilumab 200 mg alone gave better ACR20/50/70 response rates than conventional DMARDs alone
- sarilumab 200 mg alone gave similar ACR20/50/70 response rates to biological DMARDs alone.

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

- sarilumab 200 mg plus conventional DMARDs gave better ACR20/50/70 response rates than conventional DMARDs

- sarilumab 200 mg plus conventional DMARDs gave similar ACR20/50/70 response rates to the biological DMARDs plus conventional DMARDs.

The committee concluded that sarilumab works as well as biological DMARDs in moderate to severe rheumatoid arthritis that has responded inadequately to conventional or biological DMARDs.

Sarilumab monotherapy may have similar clinical effectiveness to sarilumab plus conventional DMARDs

- 3.11 The company was not able to identify any evidence on sarilumab monotherapy in patients whose disease responded inadequately to biological DMARDs. The company assumed that the efficacy of sarilumab monotherapy would be equal to that of sarilumab in combination with conventional DMARDs. The ERG noted that this assumption was reasonable but recognised the considerable uncertainty caused by the absence of direct data. The committee agreed that, in the absence of direct evidence, it is reasonable to assume sarilumab monotherapy has similar effectiveness to sarilumab plus conventional DMARDs in people whose disease has responded inadequately to biological DMARDs.

The company's network meta-analysis is suitable for decision-making

- 3.12 The ERG stated that there was some uncertainty in the methods used by the company in the network meta-analysis. Following a request by the ERG at the clarification stage, the company provided updated results using the ERG's preferred assumptions which had been used by the assessment group in [NICE technology appraisal guidance on adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for rheumatoid arthritis](#) for patients whose disease responded inadequately to conventional DMARDs. The company noted that the results of the new network meta-analysis were comparable to those of its original analyses and that the conclusion that sarilumab is comparable to other biological DMARDs was unchanged. The ERG noted that the statistically significant result for sarilumab compared with other biological DMARD treatments (both as combination therapy and monotherapy) should be treated with caution as it may be a

consequence of underestimating the uncertainty in treatment effects resulting from the use of a fixed-effects model. The committee reviewed both analyses and concluded that the methods used by the company in the network meta-analysis were in line with previous NICE technology appraisal guidance, and that the network meta-analysis was therefore suitable for decision-making.

Cost effectiveness

The company's model structure is appropriate for decision-making

3.13 The company used a patient-level Markov model for its economic evaluation. 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 which transformed ACR 20/50/70 response to EULAR response. The company analysed cost effectiveness for each of the subgroups described in [section 3.5](#). The ERG stated that the model was not an individual patient-based discrete event simulation as used by the assessment group in [NICE technology appraisal guidance on adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for rheumatoid arthritis](#). The committee noted the difference between the company's model structure and the structure accepted in the previous guidance but accepted that the company's model was appropriate for its decision-making.

The company's method for calculating utility is appropriate

3.14 The company stated that that EQ-5D utility data were not available for all comparators across all patient populations. Following a request by the ERG at the clarification stage, the company used Hernandez et al. (2013) to estimate EQ-5D data based on patient characteristics (HAQ score, pain on a visual analogue scale, age and sex). The ERG stated that Hernandez et al. was used in [NICE technology appraisal guidance on adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for rheumatoid arthritis](#). The committee

concluded it was appropriate for decision-making.

The company's methods for calculating costs are appropriate

3.15 The company's model included costs associated with drug acquisition, drug administration and monitoring, and hospitalisation. The model treatment sequences included a TNF-alpha inhibitor bundle in the base case. The TNF-alpha inhibitor bundle used the pooled efficacy of etanercept, an etanercept biosimilar, adalimumab, infliximab, an infliximab biosimilar, golimumab and certolizumab pegol with the price weighted according to the estimated market share of each. The company did not include the cost of biosimilars for rituximab or adalimumab, but stated that at the time of submission the rituximab biosimilar was not available and the adalimumab biosimilar had not received its marketing authorisation. The ERG stated that in the company's original base case the incremental cost-effectiveness ratio (ICER) for sarilumab compared with rituximab was more than £100,000 per quality-adjusted life year (QALY) gained, and so reducing the price of rituximab would not change the conclusion for this population. Sarilumab and several of the other biological DMARDs have patient access schemes. The company had incorporated the patient access scheme prices for sarilumab, certolizumab pegol and golimumab in the model, but not the confidential patient access schemes for abatacept and tocilizumab. The committee concluded that the costs used in the company's model were appropriate.

The company's updated treatment sequences are acceptable

3.16 During the clarification stage the ERG requested that the company update the sequences in which treatments are given for each subgroup to match those agreed in [NICE technology appraisal guidance on adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for rheumatoid arthritis](#). The company provided updated sequences, but the ERG noted that in the group of patients whose disease has responded inadequately to biological DMARDs, a second line of biological treatment had been added in error. This error was corrected in the ERG's additional analyses and the committee accepted this.

The ERG's changes to how patients progress from treatment for moderate disease to treatment for severe disease are appropriate

3.17 Following a request by the ERG at the clarification stage, the company updated the model to allow patients treated for moderate disease to progress to treatment for severe disease. The ERG explained that this progression, although not used in previous [NICE technology appraisal guidance on adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for rheumatoid arthritis](#), was requested because it provided a more accurate representation of clinical practice. The company updated its analyses but the ERG identified 2 issues with the company's methods:

- In the company's model patients went through a moderate treatment sequence first and then transitioned to the severe sequences only if their HAQ-DI score was above a certain threshold. The HAQ-DI score was calculated through a regression which was related to a DAS28 score of 5.1. The ERG noted that changes in HAQ-DI and DAS28 values should have been calculated instead of using absolute values because the relationship between them is not linear.
- Patients should have progressed to the severe sequences when their DAS28 score increased above 5.1, without waiting until they reached the end of the moderate sequence.

The ERG corrected these points in its additional analyses. The committee considered the changes made by the ERG and concluded that they were appropriate.

There were some concerns with how response to treatment was implemented

3.18 In the company's model patients were assessed for response to treatment at 6 months. Patients who had a moderate or good EULAR response were assumed to have an associated reduction in HAQ-DI score, which was assumed to be independent of treatment, and the treatment was stopped if the patient did not have at least moderate EULAR response at 6 months. The ERG stated that the company had used a linear approach to HAQ-DI score progression, which would have

had a favourable effect for sarilumab when compared with conventional DMARDs. It explained that a non-linear method was more appropriate and had been accepted in previous [NICE technology appraisal guidance on adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for rheumatoid arthritis](#). The ERG had used this method in its additional analyses. The committee concluded that the non-linear approach to HAQ-DI progression was appropriate and therefore accepted the ERG's additional analyses.

Cost-effectiveness results

Sarilumab with methotrexate is not cost effective for moderate disease after conventional DMARDs

3.19 In the ERG's additional analysis for the population with moderate active rheumatoid arthritis that has responded inadequately to conventional DMARDs, the ICER for sarilumab compared with conventional DMARDs was £63,438 per QALY gained. The ERG also calculated new ICERs using the confidential patient access scheme prices for abatacept and intravenous tocilizumab; this comparison produced similar estimates of cost effectiveness. The committee considered that sarilumab plus conventional DMARDs was not cost effective in people with moderate rheumatoid arthritis whose disease has responded inadequately to conventional DMARDs.

Sarilumab with methotrexate is cost effective for severe active rheumatoid arthritis after conventional DMARDs

3.20 In the ERG's additional analysis for the population with severe rheumatoid arthritis that has responded inadequately to conventional DMARDs, tocilizumab (intravenous and subcutaneous) was dominated by sarilumab plus conventional DMARDs (that is, sarilumab was both less costly and more effective). The ICERs for the TNF-alpha inhibitor bundle plus methotrexate and abatacept plus methotrexate compared with sarilumab plus methotrexate were both over £100,000 per QALY gained. The ERG also calculated ICERs using the confidential patient access scheme prices for abatacept and intravenous

tocilizumab, which produced very similar estimates of cost effectiveness. The committee therefore recommended sarilumab plus conventional DMARDs for people with severe rheumatoid arthritis whose disease has responded inadequately to conventional DMARDs, in line with the [NICE recommendations on adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept](#).

Sarilumab with methotrexate is not cost effective for severe disease after biological DMARDs if rituximab is a treatment option

3.21 In the ERG's additional analysis for the population with severe rheumatoid arthritis that has responded inadequately to biological DMARDs for whom rituximab is a treatment option, the ICER for a sequence where sarilumab plus conventional DMARDs replaced rituximab plus conventional DMARDs was over £100,000 per QALY gained. The committee concluded that sarilumab 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.

Sarilumab with methotrexate is cost effective for severe disease after biological DMARDs if rituximab is not a treatment option

3.22 In the ERG's additional analysis for the population with severe rheumatoid arthritis that has responded inadequately to biological DMARDs for whom rituximab is contraindicated, the incremental analysis for sarilumab compared with the TNF-alpha inhibitor bundle resulted in an ICER of £34,979 per QALY gained. Subcutaneous abatacept plus methotrexate was dominated by sarilumab plus methotrexate (that is, sarilumab was both less costly and more effective) and the ICERs for tocilizumab (intravenous and subcutaneous) plus methotrexate compared with sarilumab plus methotrexate were over £100,000 per QALY gained. The ERG updated its additional analysis using the confidential patient access scheme prices, which produced similar estimates of cost effectiveness. The committee therefore recommended sarilumab plus conventional DMARDs for people with

severe rheumatoid arthritis whose disease has responded inadequately to biological DMARDs and for whom rituximab is not a treatment option.

Sarilumab with methotrexate is cost effective for severe disease after rituximab and other biological DMARDs

3.23 In the ERG's additional analysis for the population with severe rheumatoid arthritis population that has not responded adequately to rituximab and other biological DMARDs, the ICER for intravenous or subcutaneous tocilizumab plus methotrexate compared with sarilumab plus methotrexate was over £100,000 per QALY gained. The ERG also updated its additional analysis using the confidential patient access scheme prices, which produced similar estimates of cost effectiveness. The committee therefore recommended sarilumab plus conventional DMARDs for people with severe rheumatoid arthritis whose disease has not responded adequately to rituximab and other biological DMARDs.

Sarilumab monotherapy is cost effective for severe active rheumatoid arthritis after conventional DMARDs if methotrexate is not suitable

3.24 In the ERG's additional analysis for the population with severe rheumatoid arthritis that has responded inadequately to conventional DMARDs for whom methotrexate is contraindicated, sarilumab alone compared with a TNF-alpha inhibitor bundle alone in the incremental analysis had an ICER of £34,422 per QALY gained. In the incremental analysis subcutaneous tocilizumab was extendedly dominated by sarilumab alone (that is, the ICER for subcutaneous tocilizumab was higher than the next more effective alternative, which was intravenous tocilizumab). The ICER for intravenous tocilizumab compared with sarilumab was over £100,000 per QALY gained. The ERG updated this additional analysis using the confidential comparator patient access scheme prices, which produced similar estimates of cost effectiveness. The committee concluded that sarilumab monotherapy is cost effective for severe active rheumatoid arthritis after conventional DMARDs if methotrexate is not suitable.

The recommendation for people whose condition has responded inadequately to biological DMARDs also applies to sarilumab monotherapy

3.25 In the ERG's additional analysis for the population with severe rheumatoid arthritis that has responded inadequately to biological DMARDs for whom methotrexate is contraindicated, the ICER for sarilumab compared with the TNF-alpha inhibitor bundle was £31,433 per QALY gained. The ERG stated that this analysis was subject to considerable uncertainty because the clinical effectiveness of sarilumab monotherapy was assumed to be equal to sarilumab in combination with conventional DMARDs. The committee acknowledged its decision that in the absence of direct evidence sarilumab monotherapy may have a similar clinical effectiveness to sarilumab plus conventional DMARDs in people whose disease has responded inadequately to biological DMARDs. The committee concluded that its recommendations for sarilumab plus conventional DMARDs in people whose disease has responded inadequately to biological DMARDs should also apply to sarilumab 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 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 determination.
- 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 rheumatoid arthritis and the doctor responsible for their care thinks that sarilumab is the right treatment, it should be available for use, in line with NICE's recommendations.
- 4.4 The Department of Health and Sanofi have agreed that sarilumab 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 GB-PatientAccess@sanofi.com.

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.

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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.

Victoria Kelly

Technical lead

Alexandra Filby

Technical adviser

Stephanie Yates

Project manager

Update information

December 2020: Recommendation 1.4 updated to clarify when sarilumab can be used as monotherapy. Recommendation 1.6 added to ensure equality when using the DAS28.

ISBN: 978-1-4731-1709-9

Accreditation

