NICE National Institute for Health and Care Excellence

NICE guidance

# Guselkumab for treating active psoriatic arthritis after inadequate response to DMARDs

Technology appraisal guidance
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# 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 replaces TA711.

# 1 Recommendations

1.1 Guselkumab, alone or with methotrexate, is recommended as an option for treating active psoriatic arthritis in adults whose disease has not responded well enough to disease-modifying antirheumatic drugs (DMARDs) or who cannot tolerate them. It is recommended only if they have had 2 conventional DMARDs and:

- have had at least 1 biological DMARD, or
- tumour necrosis factor (TNF)-alpha inhibitors are contraindicated but would otherwise be considered (as described in NICE's technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis).

  Guselkumab is recommended only if the company provides it according to the commercial arrangement. Active psoriatic arthritis is defined as peripheral arthritis with 3 or more tender joints and 3 or more swollen joints.

1.2 Assess the response to guselkumab from 16 weeks. Stop guselkumab at 24 weeks if the psoriatic arthritis has not responded adequately using the Psoriatic Arthritis Response Criteria (PsARC; an adequate response is an improvement in at least 2 of the 4 criteria, 1 of which must be joint tenderness or swelling score, with no worsening in any of the 4 criteria). If the PsARC response is not adequate but there is a Psoriasis Area and Severity Index (PASI) 75 response, a dermatologist should decide whether continuing treatment is appropriate based on skin response.

1.3 Take into account any physical, sensory or learning disabilities, or communication difficulties that could affect the responses to the PsARC and make any adjustments needed.

1.4 Take into account how skin colour could affect the PASI score and make any adjustments needed.

1.5 These recommendations are not intended to affect treatment with guselkumab 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**

People with active psoriatic arthritis that is not controlled well enough with 2 conventional DMARDs are usually offered biological DMARDs. Many of these are already recommended by NICE for treating psoriatic arthritis. Guselkumab is a biological DMARD.

Clinical evidence shows that guselkumab is effective compared with placebo, but it has not been compared directly with other biological DMARDs for treating psoriatic arthritis. An indirect comparison suggests that guselkumab is as effective as the biological DMARDs secukinumab and ixekizumab, particularly for skin symptoms.

For people who have had 2 conventional DMARDs and at least 1 biological DMARD, guselkumab's cost-effectiveness estimates are within the range that NICE normally considers an acceptable use of NHS resources.

For people who have had 2 conventional DMARDs and for whom TNF-alpha inhibitors are contraindicated, the costs and benefits are similar to those of other treatments recommended by NICE.

So, guselkumab is recommended for both of these groups.

# 2 Information about guselkumab

## Marketing authorisation indication

2.1 Guselkumab (Tremfya, Janssen), 'alone or in combination with methotrexate (MTX), is indicated for the treatment of active psoriatic arthritis in adult patients who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug (DMARD) therapy'.

## Dosage in the marketing authorisation

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

## Price

2.3 The cost of a 100 mg pre-filled disposable injection of guselkumab is £2,250.00 (excluding VAT; BNF online, accessed May 2022). The company has a commercial arrangement. This makes guselkumab available to the NHS with a discount. The size of the simple patient access scheme discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount. In the complex patient access scheme, the 4-weekly regimen is provided at the same cost as an 8-weekly regimen. If every 4 weeks dosing is needed, the price will be equalised with every 8 weeks dosing by supplying 2 of the 100 mg pre-filled disposable injections for the price of 1.

# 3 Committee discussion

The appraisal committee considered evidence submitted by Janssen, a review of this original submission by the evidence review group (ERG), another submission by Janssen for the rapid review, NICE's technical report, and responses from stakeholders. See the committee papers for full details of the evidence.

## Clinical need

### Psoriatic arthritis substantially affects health-related quality of life

3.1 The patient and clinical experts explained that active psoriatic arthritis (defined as 3 or more tender joints and 3 or more swollen joints) is a lifelong condition that seriously affects people's quality of life. It can develop at a young age, and affects a person's education, career, relationships and family life. The patient experts explained that symptoms such as fatigue, pain and associated comorbidities such as inflammatory bowel disorders, cardiovascular disease and diabetes can have a substantial physical and psychological effect. The clinical and patient experts explained that psoriatic arthritis symptoms range from mild, non-destructive disease to erosive and deforming arthritis that substantially affects daily life. Symptoms can include swollen fingers and toes, inflammation of larger joints such as elbows, knees, and back, and tendonitis. Skin and nail psoriasis also affect quality of life. The committee concluded that active psoriatic arthritis substantially affects health-related quality of life.

# Clinical management

## Clinicians and people with psoriatic arthritis would welcome additional biological treatments that target different inflammation pathways

3.2 The clinical experts explained that treatment for active psoriatic arthritis aims to control joint and connective tissue inflammation. This prevents joint damage progressing and the associated pain and disability. People will usually have treatment with non-steroidal anti-inflammatory drugs, corticosteroids, and conventional disease-modifying antirheumatic drugs (DMARDs) such as methotrexate. In line with NICE's technology appraisal guidance on etanercept, infliximab and adalimumab, people are eligible for biological or small molecule treatments if their disease is poorly controlled after 2 conventional DMARDs. Biological and small molecule treatments include:

- tumour necrosis factor (TNF)-alpha inhibitors such as etanercept and adalimumab
- interleukin (IL) inhibitors such as secukinumab and ixekizumab (IL-17A inhibitors) and ustekinumab (IL-12 and IL-23 inhibitor)
- tofacitinib
- apremilast

The clinical experts explained that psoriatic arthritis is unpredictable and can flare and change over time. Sometimes it responds to the first conventional DMARD, or to a second or third, or it may not respond at all. The clinical experts highlighted that because flares and periods of disease remission are common, the treatment pathway varies. After conventional DMARDs, people often switch among the different TNF-alpha inhibitors, or to different interleukin inhibitors (ustekinumab, secukinumab and ixekizumab) or to tofacitinib. People with psoriatic arthritis would benefit from an additional class of treatment that targets a different inflammatory mediator if:

- their disease has not responded (or has stopped responding) to DMARDs and other biologicals or small molecules, or

- they need to stop a treatment because of side effects.

Guselkumab is the first monoclonal antibody specifically targeting IL-23 to be considered by NICE for use in psoriatic arthritis. The committee concluded that people with psoriatic arthritis and clinicians would welcome a further treatment option that targets a different inflammation pathway.

# Clinical evidence

## Guselkumab is clinically effective compared with placebo

3.3 The efficacy and safety evidence for guselkumab in psoriatic arthritis comes from 2 pivotal trials, DISCOVER-1 and DISCOVER-2. These trials randomised people to have 100 mg guselkumab every 8 weeks or every 4 weeks, or to placebo. The guselkumab trial arms both showed statistically significant and clinically important benefits compared with placebo for disease activity, joint and skin symptoms, functional capacity and health-related quality of life. Guselkumab met the primary endpoint; a higher proportion of people had an American College of Rheumatology (ACR) 20 response compared with those on placebo at 24 weeks in both trials. The committee concluded that both doses of guselkumab were clinically effective compared with placebo across a range of clinically important outcomes.

## The populations in the clinical trials are broadly generalisable to NHS clinical practice and are appropriate for decision making

3.4 In its submission, the company assumed that the baseline characteristics of people in the DISCOVER trials reflected those of people seen in NHS clinical practice. The ERG explained that the DISCOVER trials did not include people from the UK. The trials recruited mainly from eastern Europe, where local health systems may have different treatment provision for psoriatic arthritis. The ERG was concerned about the generalisability of the results of the trials because of key differences in the populations compared with populations in the NHS. The company submission identified 4 subgroups and included analyses for 3 subgroups:

- people whose disease is not adequately controlled by 2 conventional DMARDs but who have not had a biological DMARD
- people whose disease is not adequately controlled by 2 conventional DMARDs or by at least 1 biological DMARD
- people whose disease is not adequately controlled by 2 conventional DMARDs and for whom TNF-alpha inhibitors (class of biological DMARD) are contraindicated.

The clinical experts confirmed the ERG's view that guselkumab was unlikely to be used as a first-line biological treatment in the NHS. So in clinical practice, a high proportion of people would have had another biological treatment before starting guselkumab. The proportion of people in the trials who had previously had a biological treatment (31% in DISCOVER-1, 0% in DISCOVER-2) did not therefore reflect NHS clinical practice. The ERG further explained that in the trials, less than a third of people had already had 2 or more conventional DMARDs. Also, just under 10% of people had not had a conventional DMARD before. Because NICE recommends that biological DMARDs are offered after 2 conventional DMARDs have been tried (see section 3.2), this further limits the applicability of the trials to the NHS. Another generalisability concern was the baseline Psoriasis Area and Severity Index (PASI) scores of people in the trials. The clinical experts agreed with the ERG that these were high and that it was rare to see people with psoriatic arthritis with PASI scores above 5 in the NHS. Because less than a third of people had 2 conventional DMARDs before starting the DISCOVER trials, it would be reasonable to expect the level of disease at baseline to be higher. The committee recalled that in previous NICE psoriatic arthritis technology appraisals, the clinical experts considered that trial PASI scores were higher than would be seen in clinical practice. The clinical experts confirmed that the populations in the trials and in the NHS were different in terms of prior treatments and disease severity at baseline. But they advised that because psoriatic arthritis is unpredictable and the available treatments do not cure it, both populations represented people with active disease. The committee agreed that:

- there were differences between the trial populations and people with psoriatic arthritis seen in NHS clinical practice

- the trial populations were broadly similar to those in comparator trials in the network meta-analyses, and to those in previous NICE psoriatic arthritis technology appraisals.

  The committee concluded that although there were differences between the populations in the trials and in the NHS, the evidence from the DISCOVER trials was broadly appropriate for including in decision making.

## The low discontinuation rates in DISCOVER-1 and DISCOVER-2 are not likely to be seen in the NHS

3.5 Discontinuation rates for the 4-weekly dose in the pivotal trials were between 2.3% (DISCOVER-1) and 3.7% (DISCOVER-2). In its submission, the company said these low rates were evidence of guselkumab's sustained efficacy, safety and tolerability. The committee recalled the ERG's and clinical experts' opinion about the differences between the trial populations and the people who would have treatment in NHS clinical practice (see section 3.4). The baseline characteristics suggested that people in the countries participating in the trials, mostly eastern Europe, had limited access to the range of treatments available in the NHS. The clinical experts explained that the low discontinuation rates in the trials, including in the placebo groups, might reflect this overall lack of access to other treatments. They added that trial discontinuation rates often do not translate into the actual rates seen in clinical practice. In the UK, people whose disease is not controlled would be expected to move quickly to another active treatment. The ERG considered that the company's justification for guselkumab's very low discontinuation rates was not robust. The ERG felt that the company had not shown an underlying biological mechanism for these low rates. The ERG rejected the company's claim that the low discontinuation rates for guselkumab (and ustekinumab) may partly be because of better skin response with these biological treatments. This was because people with psoriatic arthritis mainly have biological DMARDs to control joint disease rather than psoriasis, which tends to be less severe. Also, most studies used to inform the treatment-specific discontinuation rates for guselkumab and the comparators did not report treatment stopping rules in the maintenance period. So it was possible that people in these trials continued treatment beyond the loss of sustained response. This would

therefore not reflect the rate seen in clinical practice, where stopping rules would ensure that people did not remain on treatments that were not adequately controlling their disease. The committee agreed with the clinical experts and ERG that the trial populations and the NHS population were not similar. It also agreed about the uncertainties in the evidence base supporting the use of treatment-specific discontinuation rates. The committee concluded that the low discontinuation rates for guselkumab in DISCOVER-1 and DISCOVER-2 were not likely to be the same in the NHS.

## Early escape in the guselkumab trials results in bias

3.6 'Early escape' to another treatment is common in clinical trials and stops people staying on a treatment if they have uncontrolled disease. The clinical experts explained that it is important for ensuring people remain in trials, which improves the generalisability of the data. The company had opted to treat early escape as non-response (that is, no change from baseline) in the final analysis at 24 weeks. The ERG explained that early escape, as with treatment switching, always results in the potential for bias. Treating early escape as non-response potentially overestimates the benefit of active treatments because most early escape is expected to be in the placebo arm of trials. Early escape was only allowed after 16 weeks in the DISCOVER trials. The ERG explained that the trial investigators did not have to tell people that they had qualified for early escape. Of those who were eligible, most were in the placebo arms, and less than 50% escaped to another treatment, but the reasons for this were unclear. The ERG explained that it did not agree with the company's method of dealing with early escape in the trials, and suggested an assessment time of 16 weeks. This would mean that the data would be free of bias caused by early escape. The company re-did the network meta-analyses using 16-week data. The ERG also did an exploratory analysis of the effect on first-line treatment cost of a 16-week stopping rule. The ERG preferred an alternative approach, to include the full observed response of people who escaped early to another treatment. This would also introduce bias by assigning the benefits of an active treatment to placebo. In contrast to the company's preferred approach, this approach would potentially underestimate guselkumab's benefit and would therefore be a more conservative analysis. The company did not

consider that either of the ERG's approaches were appropriate. The company claimed that guselkumab's mechanism of action meant that it continued to be effective, particularly in measures of skin response such as PASI scores, between 16 and 24 weeks. To limit analysis to 16 weeks would therefore not represent guselkumab's full benefits. Also, it claimed that assigning guselkumab's benefits to people in the placebo arm by using the full observed response data from people who escaped early would be clinically implausible. The committee agreed with the ERG that the arguments supporting guselkumab's unique mechanism of action were not convincing and more robust evidence would be needed. The committee agreed that early escape would introduce bias for the 24-week analysis whether it was treated as non-response or the full observed response was used. The committee noted that analysing the DISCOVER trials at 16 weeks only and including the outcome data for early escape at 24 weeks reduced guselkumab's effectiveness relative to placebo, and that the company's preferred approach may have overestimated guselkumab's benefit. The committee concluded that early escape resulted in bias and that it would consider all approaches in its decision making.

## The assessment time of 24 weeks is appropriate, but clinicians would value the option of assessing response at 16 weeks

3.7 Guselkumab's summary of product characteristics states that stopping treatment should be considered when disease has not responded after 24 weeks of treatment. The patient experts explained that they welcomed the prospect of a new biological treatment that works on an additional inflammation pathway. But they also explained that people with psoriatic arthritis are frequently frustrated by having ineffective treatments, and that irreversible joint damage can occur very quickly. Many people would therefore find it difficult to accept waiting for 24 weeks to have clinical benefit assessed. The clinical experts commented that a 24-week assessment time for guselkumab was much longer than the 12- to 16-week assessment times for other biological DMARDs. They noted that continued response beyond 12 to 16 weeks had also been seen for other biological DMARDs and small molecules. The clinical experts would welcome the option to assess response at 16 weeks, to help decide whether to switch treatment or intervene with

salvage treatment. The ERG explained that it was not convinced that the evidence for guselkumab's unique mechanism of action would justify waiting until 24 weeks to assess response. It noted that the maximum Psoriatic Arthritis Response Criteria (PsARC), Health Assessment Questionnaire-Disability Index (HAQ-DI) and ACR 50 responses were recorded at week 20 in the DISCOVER trials. The ERG further explained that the company's economic model could misrepresent the quality-adjusted life year (QALY) gains associated with an improved PASI response from 16 to 24 weeks. Therefore, the model was not suitable for exploring the full effect on outcomes of using a 16-week stopping rule for guselkumab. Also, the ERG explained that it was uncertain whether an improved PASI response between 16 and 24 weeks on guselkumab was confounded by the bias potentially introduced by allowing early escape in the DISCOVER trials. The committee noted that the assessment time for skin response was 16 weeks, in line with guselkumab's marketing authorisation for moderate to severe psoriasis. The committee agreed with the ERG that the evidence for further improvement in joint disease between 16 and 24 weeks was limited. But it noted that 24 weeks was the assessment time in the summary of product characteristics. The committee concluded, however, that clinicians would value the option of assessing response at 16 weeks.

## Clinicians would value the option to continue treatment based on a PASI 75 response

3.8 Continuing guselkumab treatment depends on whether a person has a PsARC response. The ERG explored the possibility of continuing treatment when there is an inadequate PsARC response but there is a PASI 75 response. The ERG explained that this was particularly relevant for guselkumab, which is likely to produce a comparable PsARC response to other biological DMARDs, but has the highest PASI 75 response. The clinical experts explained that if a person with psoriatic arthritis and mild psoriasis did not have an adequate PsARC response, it would not be appropriate to continue guselkumab just because of a 75% reduction in their mild psoriasis. But the decision could be different for people with moderate to severe psoriasis, which can severely affect quality of life. The committee recalled the patient expert statement that for some people with psoriatic arthritis, psoriasis symptoms in skin and nails can

be hugely debilitating (see section 3.1). The patient experts also explained that the person's needs must be considered. For some people, skin and nail psoriasis symptoms can have a greater effect on quality of life than joint symptoms. The clinical experts explained that if there is only a partial PsARC response, but the person has a PASI 75 response for psoriasis that has affected their quality of life, then it may be appropriate to continue treatment while that clinical benefit lasts. Some people in this situation will continue to have slow incremental improvement in their joints over time. Clinical judgement is therefore important in deciding when to continue treatment without a full PsARC response. The clinical experts explained that about 10% to 15% of people with psoriatic arthritis present with moderate to severe psoriasis so this only affects a minority who would have guselkumab. The committee concluded that, when improvement in psoriasis symptoms benefits quality of life but there is only a partial PsARC response, clinicians would value the option to continue treatment based on a PASI 75 response.

# Network meta-analyses

## The results of the network meta-analyses are uncertain

3.9 To evaluate guselkumab's effectiveness compared with comparator treatments the company did network meta-analyses for all main outcomes, for:

- people who have not had a biological DMARD

- people who have had a biological DMARD.

  The analysis for people for whom TNF-alpha inhibitors were contraindicated was handled by removing these treatments from the analyses for people who have not had a biological DMARD before. The committee noted that all included trials were mainly comparisons with placebo, with few head-to-head comparisons of active treatments. Also, most treatments were examined either in a single trial, or a set of closely related trials from the company making the drug. For the population who have not had a biological DMARD before, guselkumab was likely the best treatment for skin symptoms, based on PASI score. But it had more modest results for other outcomes and was generally ranked inferior to TNF-alpha inhibitors, and similar to secukinumab or ixekizumab. For the population who have had a biological DMARD before, guselkumab generally ranked better, because TNF-alpha inhibitors were excluded. But the limited data meant that few comparisons (except with placebo) were conclusive. For the people for whom TNF-alpha inhibitors were contraindicated, guselkumab was the best treatment for PASI outcomes, but not clearly better than secukinumab or ixekizumab. The ERG explained that its main concern with the company's network meta-analyses was that they combined outcomes measured at different times. Comparing outcomes assessed at 24 weeks for guselkumab with outcomes assessed at 16 weeks (or earlier) for other treatments may unfairly bias results in favour of guselkumab. The ERG explained that because of the limited data, most differences in effectiveness across treatments were not conclusive. Also, the network meta-analyses results should be taken as evidence of how guselkumab broadly compares with other treatments, rather than as a robust ranking of treatments. The committee agreed with the ERG that guselkumab appeared to be very similar in effectiveness to other interleukin inhibitors (secukinumab and ixekizumab) for the endpoints included in the indirect comparison. All 3 interleukin inhibitors were ranked higher than TNF-alpha inhibitors for PASI outcomes, but lower on ACR and PsARC outcomes. The committee concluded that the results of the network meta-analyses showed treatment class effects, but the specific treatment rankings were uncertain.

# Economic model

## The model does not reflect NHS clinical practice but is

## appropriate for decision making

3.10 The committee noted that the company's model was based on that used in NICE's technology appraisal guidance on certolizumab pegol and secukinumab for treating active psoriatic arthritis after inadequate response to DMARDs. Using a Markov structure to capture all costs and outcomes associated with guselkumab and the comparators, the model included up to 3 lines of active treatment before best supportive care. The company stated that this structure was intended to reflect current treatment, where multiple lines of targeted treatment are common. The ERG confirmed that this structure was consistent with previous models used in NICE technology appraisals for psoriatic arthritis. But, using a limited number of active treatment lines does not represent NHS clinical practice. The clinical experts agreed with the ERG that because of the range of treatments and because the disease is varied and unpredictable there is no standard treatment sequence in the NHS. People will almost always start treatment with conventional DMARDs such as methotrexate, and then move onto biological DMARDs if their disease is not adequately controlled. But the exact sequence of treatments is determined by the course of the disease for each person. The committee recalled that people often switch between different biological treatments (see section 3.2). The clinical experts explained that the sequencing of biological treatments is often a mix of clinical and economic considerations. Also, there is no pathway of treatments that would suit everyone. The committee concluded that the model was limited in how well it represents clinical practice. But it agreed that the model was consistent with previous NICE technology appraisals for psoriatic arthritis and was therefore suitable for decision making.

## A 16.5% discontinuation rate should be used for all biological treatments in the economic model

3.11 The committee recalled the low discontinuation rates in DISCOVER-1 and DISCOVER-2, and the ERG and clinical experts' reasons why these may not be seen in NHS clinical practice (see section 3.5). It noted that in psoriatic arthritis appraisals published since NICE's technology appraisal guidance on etanercept, infliximab and adalimumab, a 16.5% treatment discontinuation rate had been used for all biological treatments. The ERG

explained that the treatment-specific discontinuation rates used in the company's base case were the largest driver of cost effectiveness. The ERG reiterated that the evidence supporting these different treatment-specific discontinuation rates was not robust. But it noted that even if it were, it was not appropriate to use these rates in the economic model. The ERG explained that the company's economic model allowed up to 3 lines of active treatment before people moved to best supportive care (see section 3.10). It noted that this had implications for using treatment-specific discontinuation rates. The clinical experts agreed with the ERG that people often switched between different TNF-alpha inhibitors, and to different interleukin inhibitors (ustekinumab, secukinumab and ixekizumab) or to tofacitinib. They also agreed that 16.5% was an appropriate discontinuation rate to use in the model to ensure consistency with other psoriatic arthritis technology appraisals. The ERG explained that in the company's model, people remained on treatment with best supportive care for an implausibly long time. Therefore considerable costs accrue and people's health-related quality of life declines, as their condition deteriorates. Treatment-specific discontinuation rates should only be used when the appropriate range of treatment sequences reflecting the full duration of disease are modelled. Because this was not possible in the company's model, using treatment-specific discontinuation rates introduced bias by inaccurately characterising total costs and QALYs for treatments associated with further lines of active treatment. In its response to technical engagement, the company disagreed with the ERG that treatment-specific discontinuation rates in the model could potentially bias the results in favour of longer-acting treatments like guselkumab. The company maintained that the additional time spent on guselkumab relative to other treatments before moving to best supportive care represented a real clinical benefit of guselkumab. The ERG further explained that by restricting the number of lines of treatment, the company's model was overly optimistic in quantifying the benefits of 'displacing' best supportive care. This was because it assumed that this occurred earlier than is expected in clinical practice. It also assumed that the displaced strategy would be best supportive care rather than another more cost-effective active treatment. The committee agreed that because the model could not accurately portray the range of treatment sequences used in clinical practice, using a 16.5%

discontinuation rate for all treatments would offset the risk of bias in the economic model. It would also ensure consistency with other psoriatic arthritis technology appraisals. The committee therefore concluded that a 16.5% discontinuation rate should be used for all treatments in the economic model. For the rapid review, the company's revised base case included the committee's preferred treatment discontinuation rate.

## Cost-effectiveness results by psoriasis severity were provided

3.12 The baseline PASI scores for people in the DISCOVER trials were high compared with those in people having NHS treatment (see section 3.4). The clinical experts explained that only a small proportion of people (10% to 15% of people with psoriatic arthritis; see section 3.8) present with moderate to severe psoriasis symptoms. The committee was aware that in previous psoriatic arthritis appraisals, results were presented by psoriasis subgroup. The ERG considered that this approach was appropriate. It did cost-effectiveness analyses by psoriasis severity using data from the DISCOVER trials. As part of the rapid review, the company replicated the ERG's approach and included results by psoriasis subgroup.

## The results of the comparisons with etanercept and tofacitinib should be included in the fully incremental analysis

3.13 Etanercept was included as a comparator in the scope because NICE recommends it for psoriatic arthritis, and it is commonly used in UK clinical practice (see section 3.2). After technical engagement, the company asked whether etanercept should be excluded as a comparator in the cost-effectiveness analysis because its market share was small. Also, in NICE's technology appraisal guidance on tofacitinib for treating active psoriatic arthritis, the committee decided that comparisons with best supportive care were more reliable than the fully incremental analysis. The ERG explained that both pairwise and fully incremental analyses were included in that appraisal, but the pairwise comparisons with best supportive care were considered appropriate. This was because the fully incremental analyses were very sensitive to small differences in the estimates of costs and QALYs, given that the total costs and QALYs were similar across all active treatments. The ERG

explained that the company also raised several concerns about the clinical data supporting etanercept's effectiveness, but did not provide clear evidence of bias in favour of etanercept. The committee noted that etanercept was a comparator in previous psoriatic arthritis appraisals and agreed that there was no case to support excluding it from the comparison. As part of the rapid review, the company suggested that tofacitinib is a relevant comparator for a narrower population than people who are eligible for guselkumab treatment, because of safety restrictions for JAK inhibitors that emerged during and after the original appraisal. However, the committee considered that tofacitinib is part of established NHS practice and so is a relevant comparator. The committee concluded that the results of the comparisons with etanercept and tofacitinib should be included in the fully incremental analysis.

## Additional benefits of the 4-weekly dose are uncertain, but the complex patient access scheme alleviates concerns

3.14 The committee recalled that guselkumab's 2 pivotal trials in psoriatic arthritis, DISCOVER-1 and DISCOVER-2, randomised people to 100 mg guselkumab every 8 weeks or every 4 weeks or to placebo (see section 3.3). The company's submission considered the clinical effectiveness of both the 4-weekly and 8-weekly dose but focused on the 8-weekly dose, which reflected the anticipated marketing authorisation. After technical engagement, the company told NICE that the marketing authorisation would also include a 4-weekly dose for people at high risk of joint damage. The committee was aware that there was no standard definition of 'high risk of joint damage' and that the clinical effectiveness of the 4-weekly dose provided by the company was based on its effectiveness in the full trial population, not in a high-risk population. The ERG explained that there was no evidence that effectiveness was different between the 8-weekly and 4-weekly doses after 16 weeks. It therefore considered it reasonable to assume that both doses would also have the same effectiveness for people at high risk of joint damage. The committee agreed that it could not reliably evaluate guselkumab's cost effectiveness for people at high risk of joint damage because of the uncertainty in defining the group and in the clinical evidence. However, it concluded that, despite uncertainty associated with the clinical benefit of the 4-weekly dose, the complex patient

access scheme proposed during the rapid review alleviated concerns about the cost effectiveness of the 4-weekly regimen in the populations in which the 8-weekly regimen was considered cost effective.

# Cost-effectiveness estimates

## Guselkumab is cost effective for 2 subgroups

3.15 The committee considered the cost-effectiveness analyses presented for the rapid review, which incorporated the updated confidential commercial arrangements for guselkumab. Because guselkumab and the comparators have confidential commercial arrangements, the exact incremental cost-effectiveness ratios (ICERs) are confidential and cannot be reported here. The committee considered the fully incremental and pairwise results (compared with best supportive care) for the overall subgroups (see section 3.4) and, if appropriate, further split by psoriasis severity (see section 3.12). Using the committee's preferred assumptions:

- For people whose disease is not adequately controlled by 2 conventional DMARDs and who have not had a biological DMARD, guselkumab was dominated (that is, was less effective but more costly) when considering the overall subgroup and when split by psoriasis severity.
- For people whose disease is not adequately controlled by 2 conventional DMARDs or by at least 1 biological DMARD, the fully incremental ICER for guselkumab was lower than £20,000 per QALY gained for the overall subgroup.

- For people whose disease is not adequately controlled by 2 conventional DMARDs and for whom TNF-alpha inhibitors are contraindicated, the fully incremental ICER was higher than the range normally considered a cost-effective use of NHS resources for the overall subgroup. However, the committee noted very small differences in the point estimates of costs and QALYs between guselkumab and the other treatment options for the overall subgroup. The point estimates are uncertain, and small variations either way could have a large effect on the ICER. The committee also considered the pairwise analysis with best supportive care and the net health benefit analysis in its decision making, and noted that all of the pairwise ICERs were below £30,000 per QALY gained.

  The committee concluded that guselkumab is cost effective for people who have had 2 conventional DMARDs:

- and at least 1 biological DMARD, or
- for whom TNF-alpha inhibitors are contraindicated.

# Conclusion

## Guselkumab is recommended for people who have had at least 1 biological DMARD or for whom TNF-alpha inhibitors are contraindicated

3.16 The committee acknowledged the need for further biological treatment options for people with active psoriatic arthritis. It took into account all commercial discounts for guselkumab and for other treatments in the pathway. For people with psoriatic arthritis who have had 2 conventional DMARDs and at least 1 biological DMARD, it concluded that the most plausible ICERs were within the range that NICE normally considers a cost-effective use of NHS resources. For people with psoriatic arthritis who have had 2 conventional DMARDs and for whom TNF-alpha inhibitors are contraindicated, it concluded that in the fully incremental analysis, the QALYs were similar and the incremental costs were sufficiently small between guselkumab and other biological DMARDs to allow guselkumab to be considered a cost-effective use of NHS resources. Therefore, guselkumab was recommended for people with

active psoriatic arthritis who have had 2 conventional DMARDs and have either had at least 1 biological DMARD or for whom TNF-alpha inhibitors are contraindicated but would otherwise be considered, as described in NICE's technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis.

# Other factors

## Clinicians should take into account factors that may affect the PsARC and PASI and make any clinical adjustments needed

3.17 The committee considered that the recommendation to stop treatment based on an inadequate PsARC response (in NICE's technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis) was also appropriate for guselkumab. It noted that some people may have physical, sensory or learning disabilities or communication difficulties that could affect their responses to components of the PsARC, and concluded that this should be taken into account when using the PsARC. The committee was also aware that the PASI might underestimate disease severity in people with darker skin. The committee concluded that, when using the PASI, healthcare professionals should take into account skin colour and how this could affect the PASI score and make the clinical adjustments they consider appropriate. The company raised a potential equalities issue, stating that using the PASI may create a barrier to access if clinicians were required to judge comorbid skin symptoms. This is because it obtained clinical expert advice that most rheumatologists do not use the PASI routinely. However, the updated recommendation after the rapid review does not involve using the PASI to determine treatment suitability, and the committee was satisfied that using the PASI should be routine practice and would not create inequality of access.

# 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 active psoriatic arthritis and the doctor responsible for their care thinks that guselkumab is 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 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.

**Luke Cowie and Dilan Savani**
Technical leads

**Caron Jones and Hannah Nicholas**
Technical advisers

**Kate Moore**
Project manager

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# Accreditation