

# Tildrakizumab for treating moderate to severe plaque psoriasis

Technology appraisal guidance

Published: 17 April 2019

[www.nice.org.uk/guidance/ta575](https://www.nice.org.uk/guidance/ta575)

## 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 Information about tildrakizumab .....	6
3 Committee discussion .....	7
Experience of people with psoriasis.....	7
Clinical management.....	7
Treatment pathway .....	8
Clinical evidence .....	9
Network meta-analysis.....	13
Company's economic model .....	14
Assumptions in the economic model .....	15
Utility values in the economic model .....	17
Costs in the economic model.....	18
Cost-effectiveness estimates.....	19
Other factors .....	22
4 Implementation.....	23
5 Recommendations for research.....	24
6 Appraisal committee members and NICE project team .....	25
Appraisal committee members .....	25
NICE project team .....	25

# 1 Recommendations

- 1.1 Tildrakizumab is recommended as an option for treating plaque psoriasis in adults, only if:
- the disease is severe, as defined by a total Psoriasis Area and Severity Index (PASI) of 10 or more and a Dermatology Life Quality Index (DLQI) of more than 10 and
  - the disease has not responded to other systemic treatments, including ciclosporin, methotrexate and phototherapy, or these options are contraindicated or not tolerated and
  - the company provides the drug according to the [commercial arrangement](#).
- 1.2 Consider stopping tildrakizumab between 12 weeks and 28 weeks if there has not been at least a 50% reduction in the PASI score from when treatment started.
- 1.3 Stop tildrakizumab at 28 weeks if the psoriasis has not responded adequately. An adequate response is defined as:
- a 75% reduction in the PASI score (PASI 75) from when treatment started or
  - a 50% reduction in the PASI score (PASI 50) and a 5-point reduction in DLQI from when treatment started.
- 1.4 If patients and their clinicians consider tildrakizumab to be one of a range of suitable treatments, the least expensive should be chosen (taking into account administration costs, dosage, price per dose and commercial arrangements).
- 1.5 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.
- 1.6 When using the DLQI, healthcare professionals should take into account any physical, psychological, sensory or learning disabilities, or

communication difficulties that could affect the responses to the DLQI and make any adjustments they consider appropriate.

- 1.7 These recommendations are not intended to affect treatment with tildrakizumab 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**

Treatment for moderate to severe plaque psoriasis includes systemic biological treatments for disease that does not respond to systemic non-biological treatments. Tildrakizumab is proposed as an alternative to other systemic biological treatments already recommended by NICE.

Clinical trial results show that tildrakizumab improves severe plaque psoriasis compared with placebo or etanercept. More improvement is usually seen at 28 weeks compared with 12 weeks of treatment. When compared indirectly, tildrakizumab appears to be as effective as adalimumab and ustekinumab but not as effective as other biological treatments.

The most plausible cost-effectiveness estimates for tildrakizumab compared with most other available biological treatments show that it is generally cost effective. Therefore, tildrakizumab is recommended as an option for use in the NHS for severe psoriasis that has not responded to systemic non-biological treatments, or if these are contraindicated or not tolerated.

## 2 Information about tildrakizumab

### Information about tildrakizumab

<b>Marketing authorisation indication</b>	Tildrakizumab (Ilumetri, Almirall) has a marketing authorisation 'for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy.'
<b>Dosage in the marketing authorisation</b>	<p>Tildrakizumab is administered by subcutaneous injection at a dose of 100 mg at weeks 0 and 4 and every 12 weeks thereafter. In patients with certain characteristics (for example, high disease burden, body weight of 90 kg or more), a 200 mg dose may provide greater efficacy.</p> <p>Consideration should be given to stopping treatment in patients whose psoriasis has shown no response after 28 weeks of treatment. An initial partial response may subsequently improve with continued treatment beyond 28 weeks.</p>
<b>Price</b>	<p>The list price of tildrakizumab is £3,241 for both the 100 mg (single-dose pack of 1 prefilled syringe) and the 200 mg (single-dose pack of 2×100 mg prefilled syringes) doses (excluding VAT; price as quoted in company's submission).</p> <p>The company has a <u>commercial arrangement</u>. This makes tildrakizumab available to the NHS with a discount. 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.</p>

## 3 Committee discussion

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

### Experience of people with psoriasis

#### **Psoriasis is a lifelong condition that affects all aspects of a person's life**

- 3.1 Psoriasis at any level of severity can be distressing and debilitating, affecting all aspects of life (physical, psychological, social and financial), and it is a lifelong condition. The committee noted that having treatments with few or manageable side effects, and which are effective for psoriasis on the face, hands, feet and genitals, is especially important to people with psoriasis, as is having a choice of treatments.

### Clinical management

#### **Psoriasis can be treated with topical therapies, phototherapy, and systemic non-biological and biological treatments**

- 3.2 People with plaque psoriasis may have topical therapies first line, followed by phototherapy second line. If these do not control the psoriasis, people may have systemic conventional non-biological treatments third line (such as methotrexate, ciclosporin or acitretin). If the disease does not respond to these, people may have fourth-line treatment including systemic biological treatments (such as adalimumab, brodalumab, etanercept, guselkumab, ixekizumab, infliximab, secukinumab or ustekinumab), or apremilast or dimethyl fumarate. Biosimilar versions of some biologicals are also available. The drugs are used for as long as they continue to work. If the disease no longer responds to 1 biological, people will be offered another biological. This

pattern is likely to be repeated over their lifetime. However, 1 clinical expert explained that previous biological treatments may affect the effectiveness of subsequent treatments, although there is uncertainty about the degree to which this occurs. Also, switching treatments can have a negative psychological effect on people with psoriasis. The clinical expert also stated that a variety of treatments are needed because patients can respond very differently to treatments with the same biological method of action. For people whose disease does not respond to multiple biological treatments, apremilast or dimethyl fumarate, the only remaining treatment option is best supportive care, which usually consists of topical agents and bandaging.

## Treatment pathway

### **Tildrakizumab is most likely to be used as an alternative to other systemic biological treatments**

3.3 The marketing authorisation for tildrakizumab is for 'adults who are candidates for systemic therapy'. However, in the company submission, tildrakizumab was positioned as an alternative only to systemic biological treatments, which are used after systemic non-biological treatments in current NHS practice. The positioning therefore captures a narrower population than the marketing authorisation. However, the clinical expert confirmed that this is the most likely stage in the treatment pathway at which NHS clinicians would consider using tildrakizumab. The committee concluded that this position in the treatment pathway was appropriate and that it would appraise tildrakizumab compared with other biological treatments.

### **Infliximab is a relevant comparator to tildrakizumab**

3.4 The company suggested that infliximab was not a relevant comparator because it was recommended only for people with very severe plaque psoriasis. The ERG explained that a large proportion of the population in the tildrakizumab trials (see [section 3.7](#)) had very severe plaque psoriasis. Also, infliximab was included as a comparator in previous appraisals at the same position in the treatment pathway as



tildrakizumab. The committee concluded that infliximab was a relevant comparator to tildrakizumab.

## **The most relevant comparators to tildrakizumab are other biological treatments**

3.5 The company suggested that the systemic non-biological treatments apremilast and dimethyl fumarate, used in NHS clinical practice at the same position as systemic biological treatments, were not relevant comparators. The clinical expert explained that these options were rarely used in practice because they are perceived to be less effective than biological treatments. They would only be considered for use for people for whom a biological treatment was unsuitable or who were unwilling to have a biological treatment. The committee concluded that although apremilast and dimethyl fumarate were used in the NHS for some people with psoriasis, the most relevant comparators to tildrakizumab were other biological treatments.

## **Clinical evidence**

### **The reSURFACE trials provide the key clinical evidence for tildrakizumab**

3.6 The main evidence for tildrakizumab came from the reSURFACE trials (reSURFACE 1 and reSURFACE 2). These were double-blind randomised controlled trials that included a total of 1,862 patients with plaque psoriasis. They compared 2 doses of tildrakizumab (100 mg and 200 mg) with placebo, and reSURFACE 2 also included an etanercept arm. The primary outcomes were the Psoriasis Area and Severity Index (PASI) and the Physician Global Assessment (PGA). Both PASI and PGA were assessed at 12 weeks and 28 weeks, as follows:

- PASI 75: a 75% reduction in the PASI score from when treatment started and
- PGA: a PGA rating of 'clear' (score of 0) or 'almost clear' (score of 1).

Patients in reSURFACE 1 and reSURFACE 2 were followed up for longer-term

outcomes, for 64 weeks and 52 weeks respectively.

## **The populations in the reSURFACE trials are similar to patients in the NHS who may have tildrakizumab**

3.7 The committee considered whether patients in the reSURFACE trials were similar to those in NHS clinical practice for:

- **Severity of disease:** the reSURFACE trials included patients with moderate to severe psoriasis with a PASI score of 12 or more. No minimum Dermatology Life Quality Index (DLQI) score was included. Previous NICE technology appraisals have defined severe and very severe psoriasis based on the PASI and DLQI; the PASI threshold for severe psoriasis is 10 or more.
- **Previous systemic non-biological treatment:** the committee noted that 24% of patients in reSURFACE 1 and 40% of patients in reSURFACE 2 had previous systemic non-biological treatment. The clinical expert stated that these proportions were lower than in the relevant population in NHS clinical practice. The committee was aware that subgroup analyses did not provide any evidence of a clinically relevant effect of previous systemic non-biological treatments on subsequent response to tildrakizumab.
- **Previous systemic biologicals:** the committee noted that 23% of patients in reSURFACE 1 and 13% of patients in reSURFACE 2 had previous systemic biological treatment. The ERG suggested that this might not represent NHS clinical practice at the proposed positioning of tildrakizumab. The committee recalled the clinical expert's advice that previous biological treatments may influence the effectiveness of subsequent treatments (see [section 3.2](#)). However, the committee was also aware that there was uncertainty as to the extent that this may occur, and that subgroup analyses did not provide any evidence of a clinically relevant effect of previous biological treatments on subsequent response to tildrakizumab.

The committee noted that the results of the reSURFACE trials may have overestimated the clinical effectiveness of tildrakizumab because of the proportions of patients who had not had previous non-biological and biological systemic treatment. The clinical expert advised that this would not be expected to have a large effect on the relative efficacy results. The committee concluded that the patients in the trials generally reflected those who would

have treatment with tildrakizumab in NHS clinical practice.

## **Both 100 mg and 200 mg doses of tildrakizumab are appropriate**

3.8 The company presented results for both licensed doses of tildrakizumab (100 mg and 200 mg). The company representative explained that the higher dose is intended for use from treatment induction in people with a higher body weight or disease burden, determined by the clinician. The committee noted that there was no difference in efficacy between the 2 doses in the reSURFACE trials. The clinical expert explained that clinicians would welcome flexibility in available doses of the same treatment. The committee concluded that it was appropriate to consider both licensed doses in its decision making.

## **Clinical outcomes assessed at 12 weeks and 28 weeks should be considered**

3.9 The committee was aware that tildrakizumab's marketing authorisation states that, if there is no response after 28 weeks of treatment, stopping tildrakizumab should be considered. It recalled that the PASI 75 response rate for tildrakizumab at 28 weeks was statistically significantly higher than at 12 weeks in the reSURFACE trials, and other biological treatments also had higher response rates at later assessments. The committee considered that tildrakizumab's less frequent dosing schedule meant that this late treatment effect was more noticeable because only 2 doses had been given before assessment of response at 12 weeks. The clinical expert advised that assessment at 12 weeks would be premature, and they would prefer to minimise the risk of a patient switching from a potentially effective treatment (see [section 3.2](#)). The committee concluded that the clinical outcomes from the reSURFACE trials at weeks 12 and 28 should be considered in its decision making.

## **Tildrakizumab is more clinically effective than placebo or etanercept**

3.10 The committee noted that:

- At week 12, patients randomised to tildrakizumab were more likely to have a PASI 75 and PGA clear or minimal response than patients randomised to placebo or etanercept.
- At week 28, patients randomised to tildrakizumab were more likely to have a PASI 75 and PGA clear or minimal response than those randomised to etanercept, but no information compared with placebo was available.

The committee concluded that tildrakizumab was more clinically effective than placebo and etanercept.

## **Assess response to tildrakizumab before and at 28 weeks, and consider stopping treatment if there is no response**

3.11 Based on consultation comments, the committee understood that clinicians may find it unreasonable to continue tildrakizumab for 28 weeks for patients whose psoriasis is not responding to treatment. The committee recalled that, in the reSURFACE trials, patients whose disease had not had at least a 50% reduction in the PASI score at 12 weeks were less likely to have a PASI 75 response at 28 weeks than patients whose disease had partially responded at 12 weeks (PASI 50). The committee also recalled that most patients whose psoriasis had a PASI 75 response reached this outcome by week 22, after taking the third dose in week 16. It was aware that no similar data were presented for other outcomes such as DLQI. The committee considered that although stopping treatment from 14 weeks was considered in the economic modelling (see [section 3.17](#)), it was more appropriate to consider stopping treatment from 12 weeks. This was because this reflected the trial data and was in line with previous NICE technology appraisal guidance, such as [NICE's technology appraisal guidance for etanercept efalizumab for the treatment of adults with psoriasis](#), [brodalumab for treating moderate to severe plaque psoriasis](#), [ixekizumab for treating moderate to severe plaque psoriasis](#) and [secukinumab for treating moderate to severe plaque psoriasis](#). The committee concluded that if there was no adequate response at 28 weeks (either a PASI 75 response, or a PASI 50 response and a 5-point reduction in DLQI), tildrakizumab should be stopped (see [section 3.9](#)). Also, if there has not been at least a 50% reduction in the PASI score from when treatment

started between 12 weeks and 28 weeks, stopping tildrakizumab should be considered.

## Network meta-analysis

### The network meta-analysis including infliximab is appropriate for decision making

3.12 The company did a network meta-analysis to indirectly compare tildrakizumab with other biological treatments (adalimumab, brodalumab, etanercept, guselkumab, ixekizumab, secukinumab and ustekinumab) using data from 45 trials. The included trials assessed PASI 75 response at various time points, which the company grouped into separate stages for its analysis:

- Response measured at 12 weeks to 16 weeks (stage I).
- Response measured at 16 weeks to 24 weeks (stage II). Stage II was a separate planned analysis that excluded the placebo arms, resulting in an incomplete network, therefore it was not considered in this appraisal.
- Response measured at 24 weeks to 28 weeks (stage III).

No trials reported placebo outcomes at stage III. To include placebo in its stage III network, the company used placebo response rates from the same trials at stage I. The ERG noted that this made the stage III analysis weaker than the stage I analysis. This was because there were no direct placebo data at 24 weeks to 28 weeks, and because most trials were open label at this point, although a stage III etanercept control group was included. The ERG also advised that excluding infliximab from the network was inconsistent with previous appraisals, and that including it would strengthen the network. The ERG therefore included 6 additional trials in an exploratory analysis. The committee concluded that the network meta-analysis, including infliximab, was appropriate for decision making. The company accepted the committee's preference and the ERG's exploratory analysis.

## **Tildrakizumab is more effective at 28 weeks than at 12 weeks**

- 3.13 For the stage I (12 weeks to 16 weeks) analysis, the committee noted that the PASI 75 response rates for tildrakizumab were higher than those for etanercept, similar to adalimumab and ustekinumab, and lower than for other targeted biological treatments, including guselkumab (an interleukin-23 inhibitor, as is tildrakizumab). For the stage III (24 weeks to 28 weeks) analysis the committee noted that the network meta-analysis suggested that the PASI 75 response rates for tildrakizumab were statistically significantly higher than at stage I. It also noted that tildrakizumab at stage III had a higher PASI 75 response rate than etanercept and adalimumab at stage III, and similar efficacy to other targeted biological treatments at stage I, which reflected the stopping rules used in NHS practice for those treatments. The committee concluded that tildrakizumab was more effective at stage III than at stage I. It also concluded that the efficacy of tildrakizumab at stage I was closest to adalimumab at stage I, and the efficacy of tildrakizumab at stage III was closest to guselkumab at stage I.

## **Company's economic model**

### **The model has a Markov state transition structure**

- 3.14 A Markov state transition model was used to assess the cost effectiveness of tildrakizumab. It assumed that treatments improved quality of life but did not extend length of life. The model contained 4 health states: induction treatment, maintenance treatment, best supportive care and death. All patients entered the model in the induction state and had the first treatment in a given sequence (see [section 3.15](#)). They moved from the induction state to the maintenance state if there was at least a PASI 75 response measured at the end of induction. From there, some patients could stop treatment for any reason and move to the next treatment in the sequence. If there was not a PASI 75 response, patients moved to the induction phase of the next treatment in the sequence. Patients moved to the best supportive care state if their psoriasis did not respond to the last active treatment in a sequence. All patients could move to the death state at any time.

## The company's model compares treatment sequences

3.15 The company's decision problem compared a sequence of treatments including tildrakizumab with 7 other sequences excluding tildrakizumab. Each sequence comprised 4 treatments:

- The first treatment was either tildrakizumab or another biological treatment (adalimumab, brodalumab, etanercept, guselkumab, ixekizumab, secukinumab or ustekinumab).
- The second treatment was ustekinumab, except in the sequence in which ustekinumab was used as the first treatment; in that sequence, adalimumab was used as the second treatment.
- The third treatment was secukinumab, except in the sequence in which secukinumab was used as the first treatment; in that sequence, adalimumab was used as the third treatment.
- The fourth treatment in all sequences was best supportive care.

The company chose these sequences based on expert advice. The committee was aware that, over time, a sequence of biologicals would be used to treat severe psoriasis in current NHS practice because people switch from 1 option to another. It was also aware that additional factors should be considered when comparing treatment sequences, such as the best ordering of treatments and the effect of including treatments that may not be cost effective. The committee agreed that, in principle, it was appropriate to compare treatment sequences in this appraisal.

## Assumptions in the economic model

### A common 14-week induction period is inappropriate

3.16 The company included a common 14-week induction period for tildrakizumab and all comparators in its economic model. The company explained that this was to simplify the model, and that a 14-week induction period was chosen to represent the midpoint of the range of typical induction periods (stage I from the network meta-analysis;

12 weeks to 16 weeks). The ERG explained that this method would create bias in the costs of the induction period. So, it explored a scenario of modelling treatment-specific induction period costs to reflect the recommended induction duration of each one. The committee recognised that a common 14-week induction period was particularly inconsistent with a potential 28-week induction period for tildrakizumab (see [section 3.11](#)). The committee concluded that assuming a common induction period could apply to treatments with different induction durations was inappropriate. It therefore preferred the ERG's modelling of treatment-specific induction period costs. The company subsequently provided a revised base case in which treatment-specific induction costs were used.

## **Tildrakizumab is compared with the induction periods used in current practice for other biological treatments**

3.17 The company included a scenario analysis in its submission comparing the cost effectiveness of tildrakizumab with a 28-week induction period with all other treatments at 28 weeks. The ERG noted that no other treatments had a recommended assessment time in the stage III time range, and so the appropriate comparison would be with treatments at their recommended assessment times. The ERG therefore included tildrakizumab with 14-week and 28-week induction periods as separate interventions in its exploratory analysis. The committee recalled that the network meta-analyses showed a statistically significant improvement in the PASI 75 response rate for tildrakizumab between the 2 assessment points (see [section 3.13](#)). The committee concluded that it preferred the ERG's approach; namely, that tildrakizumab with a 14-week and a 28-week induction period should be compared with other biological treatments at their recommended 12-week to 16-week induction periods, to reflect the stopping rules used in NHS practice for those treatments. The company subsequently provided a revised base case in which tildrakizumab with a 14-week and a 28-week induction period was compared with other biological treatments at their recommended 12-week to 16-week induction periods.



## Utility values in the economic model

### **The company's utility values are appropriate, without adjustment for age**

3.18 The company used EQ-5D data collected in the reSURFACE 1 trial to inform utility values in its economic model. Utility values were stratified by the level of PASI response. The company implemented its utility values in the economic model by assuming a percentage change from general age-related population values. The ERG suggested that adjusting utility values for age in this way may be inappropriate because it assumes a constant relationship between age and PASI score. It also noted that, because no extension of life for any treatment had been modelled, adjusting for age added a complexity to the model that was not needed. The committee concluded that the ERG's scenario analysis using the company's absolute utility values without adjusting for age was more appropriate. The company subsequently provided a revised base case in which absolute utility values without adjusting for age were used.

### **Best supportive care utility values should return to baseline**

3.19 The company assumed, in its model, that the utility value for patients having best supportive care was equal to the utility value associated with the lowest PASI reduction (less than 50%). The clinical expert considered this to be inappropriate, advising that a patient who switched from an active treatment to best supportive care would revert to their baseline quality of life shortly after switching. The ERG noted limitations in stratifying utility value by PASI response; namely, a person with a PASI response below 50% might still have some improvement in their PASI that has a positive effect on quality of life, and that PASI response may not fully capture improvements in the psoriasis from treatment. This may explain why the utility value for the 'PASI response less than 50%' group was notably higher than the baseline value. The ERG did an exploratory analysis using the baseline utility value for those having best supportive care. The committee concluded that the baseline utility value was more appropriate for representing health-related quality of life than the utility value for patients whose psoriasis had the lowest response to treatment.

The company subsequently provided a revised base case in which baseline utility values were used for patients having best supportive care.

## Costs in the economic model

### The ERG's drug costs and resource use estimates are appropriate for decision making

3.20 The company presented drug costs adjusted for a 14-week induction period and annual maintenance costs adjusted for a 14-week cycle length. The ERG revised these costs for each treatment-specific induction period (see [section 3.16](#)) and corrected maintenance costs. Biosimilar price reductions for etanercept were considered by the company. The ERG included additional healthcare costs for those whose psoriasis did not respond to biological treatments, increasing the company's one-off switching costs to reflect a 14-week cycle cost. The committee concluded that the ERG's amendments to costs and resource use were appropriate for decision making. The company subsequently provided a revised base case using the ERG's amendments to costs and resource use.

### The costs of best supportive care are uncertain

3.21 In its model, the company included the costs of best supportive care from [NICE's guideline on psoriasis: assessment and management](#), which includes drug treatment, day centre care and inpatient care. Previous psoriasis appraisals obtained direct costs from an observational study (Fonia et al. 2010). The ERG advised that the costs of best supportive care from this source, used in previous appraisals, were considerably lower than the company's estimate from the psoriasis guideline. The ERG advised that, despite being lower than the company's estimates, the costs in Fonia et al. may still have overestimated the true costs of best supportive care in NHS practice because the secondary care resource use in the study appeared to be high. The committee concluded that the costs of best supportive care for people whose psoriasis does not respond to treatment is uncertain because of a lack of recent studies to quantify the true costs in clinical practice. It concluded that, for this

appraisal, the Fonia et al. costs should be used because they are more likely to reflect current clinical practice than the costs used in the company's model, and this is consistent with previous appraisals. The company subsequently provided a revised base case using the Fonia et al. best supportive care costs. The committee further concluded that defining costs associated with psoriasis that reflect current clinical practice was an important area for research.

## Cost-effectiveness estimates

### Treatment sequences may result in misleading cost-effectiveness estimates

3.22 The committee was aware that treatment sequences, although more likely to reflect the treatment switching seen in clinical practice, may have provided misleading cost-effectiveness estimates for tildrakizumab. It noted that some of the treatments were not cost effective in the model. Therefore, the cost effectiveness of any new treatment included early in these sequences would likely be driven by avoiding potentially cost-ineffective subsequent treatments or by choosing treatments with lower response rates, resulting in an earlier transition to best supportive care. The committee was also aware that the company's model compared a limited number of all potential treatment sequences. The ERG compared individual treatments with best supportive care in its own base case, setting the second and third options in all sequences to best supportive care. The committee concluded that it would consider these comparisons of individual treatments with best supportive care in its decision making to account for potential bias caused by analysing treatment sequences. The company subsequently provided a revised base case with pairwise comparisons of individual treatments with best supportive care.

### Considering incremental net monetary benefit in addition to ICERs is appropriate for decision making

3.23 The company did a fully incremental analysis of treatment sequences, using the cheapest biological treatment (etanercept) as a baseline. The

committee noted that several treatments had only small differences in total costs and quality-adjusted life year (QALY) gains, and that these small differences could be difficult to see using incremental cost-effectiveness ratios (ICERs) from fully incremental or pairwise analyses. The ERG therefore presented the cost-effectiveness results in a net monetary benefit framework. The incremental net monetary benefit of each comparator was compared with best supportive care at opportunity costs of £20,000 and £30,000 per QALY gained. The committee concluded that incremental net monetary benefit was useful in determining the relative cost effectiveness of the interventions with similar costs and QALYs, and that it should be considered alongside the company's and the ERG's ICERs. The company subsequently provided a revised base case, which included results presented in a net monetary benefit framework.

## **Tildrakizumab is more cost effective than other biological treatments**

3.24 The committee considered whether tildrakizumab would be a cost-effective use of NHS resources for people with severe psoriasis for whom biological treatments are an option, taking into account a revised patient access scheme for tildrakizumab and the patient access schemes for the other biological treatments. The committee considered deterministic results from the company's revised analyses as adjusted by the ERG to take into account the patient access schemes for brodalumab, guselkumab, ixekizumab and secukinumab. The revised analyses included results of comparisons between treatment sequences (see [section 3.15](#)) as well as results of pairwise comparisons of individual treatments with best supportive care (see [section 3.22](#)). The revised analyses used the committee's preferred utility values (see [section 3.18](#) and [section 3.19](#)), cost estimates (see [section 3.20](#) and [section 3.21](#)) and induction period durations (see [section 3.16](#) and [section 3.17](#)).

- For tildrakizumab assessed at 28 weeks, its QALY gain compared with best supportive care was closer to the QALY gains of other targeted treatments that are usually assessed between 12 weeks to 16 weeks (such as brodalumab, guselkumab, ixekizumab, infliximab and secukinumab). The committee agreed that this meant that tildrakizumab, when assessed at 28 weeks, could

potentially displace these treatments. The committee therefore considered the cost-effectiveness estimates for tildrakizumab assessed at 28 weeks compared with these comparators. It noted that, although other biological treatments were more expensive and more effective, tildrakizumab provided one of the highest net benefits compared with best supportive care (more than £7,000 at an opportunity cost of £20,000 per QALY gained, compared with less than £6,000 for the comparators) and was therefore considered cost effective. The committee concluded that tildrakizumab assessed at 28 weeks was likely to be a cost-effective use of NHS resources.

- The committee then considered whether tildrakizumab would be cost effective with a shorter induction period (14 weeks). The QALY gain compared with best supportive care was lower than when assessed at 28 weeks and lower than the QALY gain of most other biological treatments. However, tildrakizumab had a higher net benefit compared with best supportive care (around £7,000) than many other NICE approved biological treatments, such as ixekizumab, guselkumab and secukinumab compared with best supportive care (less than £6,000). The committee, therefore, concluded that tildrakizumab assessed at 14 weeks was likely to be a cost-effective use of NHS resources.

The committee concluded that tildrakizumab was likely to be a cost-effective use of NHS resources when response was assessed either at 14 or 28 weeks. However, tildrakizumab with a 28-week stopping rule produced a higher QALY gain than with a 14-week stopping rule and had a higher net benefit. The committee, taking into account the considerations mentioned in [section 3.9](#), concluded that if there was no adequate response at 28 weeks (either a PASI 75 response, or a PASI 50 response and a 5-point reduction in DLQI) tildrakizumab should be stopped. The committee also concluded that, if there had not been at least a 50% reduction in the PASI score from when treatment started to between 12 and 28 weeks, stopping tildrakizumab should be considered (see [section 3.11](#)).

## Other factors

### The PASI and DLQI may not be appropriate for all people with psoriasis

3.25 The committee noted, as in previous NICE technology appraisal guidance on psoriasis, potential equality issues:

- the PASI might underestimate disease severity in people with darker skin
- the DLQI has limited validity in some people, and may miss anxiety and depression

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. Also, it concluded that, when using the DLQI, healthcare professionals should take into account any physical, psychological, sensory or learning disabilities, or communication difficulties, that could affect the responses to the DLQI and make any adjustments they consider appropriate.

### Tildrakizumab is not innovative

3.26 The committee understood that tildrakizumab is an interleukin-23 inhibitor with a 12-week dosing schedule. The committee was aware that the 12-week interval between doses is longer than for most other biological treatments currently available in NHS practice. The clinical expert advised that this would be welcomed by patients as a less burdensome treatment option. The committee concluded that, although less frequent dosing may reduce the burden to people with psoriasis, it was unlikely that there were additional gains in health-related quality of life over those already included in the QALY calculations.

## 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 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 psoriasis and the doctor responsible for their care thinks that tildrakizumab is the right treatment, it should be available for use, in line with NICE's recommendations.

## 5 Recommendations for research

5.1 The committee noted that the costs of best supportive care are derived from a study published in 2010 and that clinical practice has changed substantially since then. It therefore considered that it would be valuable to have studies investigating:

- the costs associated with best supportive care
- resource use, including frequency and length of hospitalisation, and associated costs.



## 6 Appraisal committee members and NICE project team

### Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by [committee B](#).

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.

#### **Adam Brooke, Iordanis Sidiropoulos**

Technical leads

#### **Jamie Elvidge, Ross Dent**

Technical advisers

#### **Jeremy Powell**

Project manager

ISBN:978-1-4731-3366-2