# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Draft guidance consultation

# Secukinumab for treating moderate to severe hidradenitis suppurativa

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using secukinumab in the NHS in England. The evaluation committee has considered the evidence submitted by the company and the views of non-company stakeholders, clinical experts and patient experts.

**This document has been prepared for consultation with the stakeholders.** It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from the stakeholders for this evaluation and the public. This document should be read along with the evidence (see the committee papers).

The evaluation committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of age, disability, gender reassignment, pregnancy and maternity, race, religion or belief, sex or sexual orientation?

**Note that this document is not NICE's final guidance on secukinumab. The recommendations in section 1 may change after consultation.**

After consultation:

- The evaluation committee will meet again to consider the evidence, this evaluation consultation document and comments from the stakeholders.
- At that meeting, the committee will also consider comments made by people who are not stakeholders.
- After considering these comments, the committee will prepare the final draft guidance.
- Subject to any appeal by stakeholders, the final draft guidance may be used as the basis for NICE's guidance on using secukinumab in the NHS in England.

For further details, see NICE's manual on health technology evaluation.

The key dates for this evaluation are:

- Closing date for comments: 19 July 2023
- Second evaluation committee meeting: 2 August 2023
- Details of the evaluation committee are given in section 4

# 1 Recommendations

1.1 Secukinumab is not recommended, within its marketing authorisation, for treating active moderate to severe hidradenitis suppurativa (acne inversa) in adults when the disease has not responded well enough to conventional systemic therapy.

1.2 This recommendation is not intended to affect treatment with secukinumab that was started in the NHS before this guidance was published. People having treatment outside this recommendation 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

Current treatment for people with moderate to severe hidradenitis suppurativa when conventional systemic therapy has not worked well enough is adalimumab. The company has positioned secukinumab for people who cannot have adalimumab or whose condition has not responded to adalimumab. This is a narrower population than secukinumab is licensed for.

Evidence from 2 clinical trials shows that secukinumab generally improves symptoms of moderate to severe hidradenitis suppurativa more than placebo. The trials did not use the same treatments alongside secukinumab or placebo that are usually used for hidradenitis suppurativa in UK clinical practice. So, the benefit of secukinumab is unclear. Also, both trials are short so the longer-term effect of secukinumab is also unclear.

The cost-effectiveness estimates are all above what NICE considers an acceptable use of NHS resources. So, secukinumab is not recommended.

# 2 Information about secukinumab

## Marketing authorisation indication

2.1 Secukinumab (Cosentyx, Novartis) does not have a marketing authorisation in Great Britain yet. It received a marketing authorisation by the European Commission for the treatment of 'active moderate to severe hidradenitis suppurativa (acne inversa) in adults with an inadequate response to conventional systemic hidradenitis suppurativa therapy'.

## Dosage in the marketing authorisation

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

## Price

2.3 The list price of secukinumab is £1,218.78 per 300 mg/2 ml solution for injection pre-filled pen, or per 2 x 150 mg/1 ml solution for injection pre-filled pens (excluding VAT; BNF online accessed April 2023). The company has a commercial arrangement. This makes secukinumab available to the NHS with a discount and it would have also applied to this indication if the technology had been recommended. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

# 3 Committee discussion

The evaluation committee considered evidence submitted by Novartis, a review of this submission by the external assessment group (EAG), and responses from stakeholders. See the committee papers for full details of the evidence.

## The condition

### Background

3.1 Hidradenitis suppurativa (HS) is a painful, long-term skin condition that causes abscesses and scarring. The exact cause of HS is unknown but it

occurs in skin folds where there are sweat glands, in particular the groin and armpits. It affects about 1 in 100 people and is more common in women than men. Symptoms of HS can range from mild to severe. Early symptoms include isolated, painful nodules; with or without intermittent inflammation. Symptoms may progress to abscesses and pus-discharging tunnels, known as sinus tracts and fistulas. The extent and severity of HS are often determined using the Hurley staging system. The focus of the company's submission is moderate (Hurley stage 2) to severe (Hurley stage 3) HS.

## Clinical and patient perspectives

3.2 Clinical experts attending the committee meeting explained that HS is a chronic, inflammatory condition. Some people will have periods where symptoms may improve or worsen over weeks or months. However, in some people, HS progresses from mild to moderate to severe without periods of improvement. Severe HS is characterised by a build-up of skin changes including abscesses, lesions and tunnels underneath the skin. These skin changes are often associated with chronic discharge of pus and blood. Clinical experts at the committee meeting and the patient expert statement explained that HS has a substantial impact on people's quality of life. The patient expert statement described severe pain, intense itching and the burden of living with chronic, inflamed and draining wounds. The statement noted that the unpredictable onset and duration of symptoms mean that living a normal life is difficult. Clinical experts at the committee meeting and the patient expert statement described how the condition affects career prospects, family relationships and the decision to have children. The patient expert statement explained that people with HS often experience anxiety and depression. Clinical experts explained that if HS is not well controlled with medication then major surgery is needed, which requires several months of recovery. The committee noted that data from a real-world, prospective study of 1,299 people with HS globally (the Global VOICE study) found that around 46% of people with moderate to severe HS were not satisfied with their current treatments because of poor

efficacy and side effects. The committee concluded that moderate to severe HS has a substantial burden on quality of life, and alternatives to surgery and existing biological treatment are needed.

## Clinical management

### Current treatment pathway

3.3 Guidelines published by the British Association of Dermatologists recommend starting treatment for HS with conventional systemic therapy. This includes offering oral tetracyclines for at least 12 weeks followed by oral clindamycin and rifampicin when oral tetracyclines have not worked. The guidelines recommend that retinoids such as acitretin or the anti-inflammatory antibiotic, dapsone, may be considered when earlier treatments have not worked. Clinical experts explained that people often cycle through multiple courses of tetracycline antibiotics but these rarely control moderate to severe disease. They also explained that every person is different, and the types of treatments offered in clinical practice are tailored to the individual. NICE's technology appraisal on adalimumab for treating moderate to severe hidradenitis suppurativa (from now, TA392) recommends adalimumab for moderate to severe HS in adults whose disease has not responded to conventional systemic therapy. The clinical experts explained that almost all people with moderate to severe HS will be offered adalimumab. A small number of people are contraindicated to adalimumab and some people prefer not to have it. Of the people who do have adalimumab, it sometimes does not work well enough or at all. In the PIONEER studies, which assessed adalimumab compared with placebo in people with moderate to severe HS, about half of people had a clinical response at week 12. Clinical response was defined as at least a 50% reduction from baseline in the abscess and inflammatory-nodule count, with no increase in abscess or draining fistula counts. Adalimumab may also work at first but then stop working, which is described as secondary failure. Clinical experts explained that adalimumab may be supplemented with other treatments if symptoms start to worsen. TA392 recommends that response to adalimumab should

be assessed after 12 weeks, and treatment should only be continued if there is clear evidence of response. In this context, response is defined as:

- a reduction of 25% or more in the total abscess and inflammatory nodule count and
- no increase in abscesses and draining fistulas.

In current clinical practice, people whose disease does not respond to adalimumab will be offered best supportive care (BSC). The company assumes that BSC includes surgical procedures, antibiotics, retinoids, dapsone, ciclosporin and anti-androgens. Clinical experts noted some limitations with these treatments. Dapsone is rarely used because it needs extensive monitoring for haemolytic anaemia. Rifampicin may be used but has many drug interactions. Retinoids, such as acitretin, may be offered as monotherapy or in combination with antibiotics, but these are contraindicated for people of childbearing age. The clinical experts also highlighted the role of weight loss and surgery in managing HS. They explained that people with HS tend to be overweight and there is evidence to show that weight loss can also lead to clinical improvement and increased efficacy of treatments. Also, surgery is generally only suitable for people with a body mass index below 35 kg/m$^2$. The clinical experts added that although surgery may be helpful, it is limited to a specific area of the body and does not prevent disease progression in other areas. The types of surgery that people with HS often have are discussed further in section 3.16. The committee concluded that the treatment pathway presented by the company, based on British Association of Dermatologists' guidelines, broadly reflects treatments given in NHS practice, but treatment is tailored according to the individual.

## Positioning of secukinumab

3.4 The marketing authorisation for secukinumab is for active moderate to severe HS in adults when the condition has not responded well enough to conventional systemic therapy. The company has positioned

secukinumab for active moderate to severe HS in people who cannot take adalimumab, including those for whom adalimumab did not work or stopped working. This is a narrower population than covered by the marketing authorisation. The comparator in the company's submission is BSC, which includes surgical procedures, antibiotics, retinoids, dapsone, ciclosporin and anti-androgens. Clinical experts noted some limitations with the company's BSC treatments (see section 3.3). Clinical experts added that the proportion of people for whom adalimumab is contraindicated is small, but adalimumab treatment is often not effective so alternatives are needed. The committee concluded that the company's positioning of secukinumab in the treatment pathway was appropriate, but noted that clinical data was not aligned with the intended positioning (see section 3.7).

## Clinical effectiveness

### SUNNY trials

3.5 The company presented evidence from 2 identically designed, phase 3, randomised, double-blind, placebo-controlled, parallel-group trials: SUNSHINE (n=541) and SUNRISE (n=543). These trials are collectively known as the SUNNY trials. The trials compared secukinumab 300 mg subcutaneously every 2 weeks or every 4 weeks with matched placebo in adults with moderate to severe HS. The study duration was 52 weeks, but comparative effectiveness data was not available after week 16 because people in the placebo arm of the trial were re-randomised to have secukinumab. The primary outcome of the trials was the proportion of people with an HS clinical response score of 50 (HiSCR50) at week 16. HiSCR50 is defined as at least a 50% decrease in abscess and inflammatory nodule count with no increase in the number of abscesses or draining fistulas. Secondary outcomes included percentage change in abscess and inflammatory nodule count, proportion of people with HS flares and the number of people achieving numerical rating scale of 30 (NRS30); which is a measure of skin pain. All secondary outcomes were also assessed at week 16. For the primary outcome, the proportion of

people with HiSCR50 was higher for secukinumab compared with placebo across both trials and doses. In SUNSHINE, 45.0% of people on secukinumab every 2 weeks had disease response compared with 41.8% of people on secukinumab every 4 weeks and 33.7% of people on placebo. In SUNRISE, the corresponding response percentages were 42.3%, 46.1% and 31.2%. The differences compared with placebo were statistically significant across both trials and treatment arms except for the secukinumab every-4-weeks arm of SUNSHINE. For secondary outcomes, there was a reduction in skin pain, a decrease in abscess and inflammatory nodule count and fewer people experienced HS flares on both doses of secukinumab compared with placebo. But this difference was not always statistically significant across treatment arms and trials. The committee noted that response rates were not always higher for people having secukinumab every 2 weeks, compared with every 4 weeks. So, it was not clear that a dose-response relationship exists for secukinumab in HS. The committee considered that the relatively high response rates seen in the placebo arm may suggest that some people entered the trial with more severe HS that spontaneously improved (regression to the mean). The committee also heard from clinical experts that in severe HS it can be difficult to accurately and objectively measure the extent and severity of disease using HiSCR. This is because it can be challenging to count the number of fistulas in severe disease. The committee concluded that it was plausible that secukinumab improved outcomes compared with placebo.

## Generalisability of population to decision problem

3.6 The company is positioning secukinumab for moderate to severe HS in people who cannot take adalimumab or in people for whom adalimumab did not work or stopped working (see section 3.4). The EAG noted that the SUNNY trials included people with moderate to severe HS, irrespective of whether they had previous adalimumab treatment. Around 23% of people in the SUNNY trials had previously had systemic biological therapy, mostly with adalimumab. The EAG was concerned that the overall

population of the SUNNY trials does not match the company's positioning of secukinumab as a second-line biological treatment after adalimumab. The EAG noted that adalimumab and secukinumab use a different mechanism of action, so non-response to adalimumab would not necessarily impair the response to secukinumab. However, secukinumab is likely to be used in practice in more difficult to treat HS that is unresponsive to adalimumab. So, the effect size seen with secukinumab in the trials may be greater than that seen in practice. Pre-specified subgroup analyses of the SUNNY trial data showed that achieving HiSCR50 at week 16 was broadly consistent in groups with and without previous exposure to biologicals. The odds ratio for the every-2-weeks dose was 1.60 for those who had previous biologicals, compared with 1.64 for the group who did not, and for the every-4-weeks dose was 1.67 compared with 1.61, respectively. The committee was initially concerned that there may be differences between those who had simply had previous adalimumab and those in whom previous adalimumab had failed. After the committee meeting, the committee noted that most of the people in the SUNNY trials who had previous biologicals stopped them because of a lack of efficacy. The committee considered that there were some uncertainties about whether the SUNNY trials were generalisable to the decision problem. But on balance, the committee concluded that the results of the full trial population, including people who had previous biologicals and those who did not, were generalisable to the company's narrower target population of people with moderate to severe HS who cannot take adalimumab, including those for whom adalimumab did not work or stopped working.

## Generalisability of BSC treatments in SUNNY trials to NHS clinical practice

3.7 People in the SUNNY trials were allowed to have concomitant medication alongside secukinumab or placebo. The trial protocols allowed simple pain management and restricted use of antibiotics as concomitant

treatments. However, the clinical experts noted the broad range of treatment options that are offered to people with HS in UK clinical practice, including surgery (section 3.3). The clinical experts added that the evidence base for treatments typically given as BSC in clinical practice is poor. One clinical expert noted after the meeting that the British Association of Dermatologists is currently setting up an HS registry for the UK and Ireland (H-STRONG). The registry will collect pharmacovigilance and real-world efficacy data for the new HS treatments. It will also function as a prospective cohort study to identify markers of rapid disease progression. The committee concluded that concomitant treatments in the SUNNY trials were more restrictive than those offered to people in clinical practice. So, it is possible that people having the BSC treatments permitted in the SUNNY trials will have worse efficacy outcomes than people having BSC in clinical practice. This may favour secukinumab.

## Long-term efficacy

3.8 As discussed in section 3.5, the SUNNY trials provided 16 weeks of comparative effectiveness evidence for secukinumab and placebo. After week 16, people in the placebo arm of the trial were re-randomised to have secukinumab. The clinical experts noted that response rates increased by around 5% to 25% between week 16 and week 52 across treatment arms and doses. The clinical experts considered that this was encouraging regarding the long-term effectiveness of secukinumab. The EAG noted that the follow-up duration of the SUNNY trials was short. The company submission and one clinical expert at the committee meeting also noted that, because HS is a progressive disease, it would be unethical for people in the trial to have placebo for longer than 4 weeks.

The committee concluded that the lack of long-term clinical effectiveness data contributed to uncertainty about the cost-effectiveness estimates.

## Economic model

### Company's modelling approach

3.9 The company developed a Markov model with 5 health states based on HiSCR score. The model was aligned with the model used for adalimumab in NICE's technology appraisal guidance on adalimumab for treatment moderate to severe hidradenitis suppurativa. The model health states included:

- no response (HiSCR score of less than 25)
- partial response (HiSCR score of 25 to 49)
- response (HiSCR score of 50 to 74)
- high response (HiSCR score of 75 and over), and
- death.

People in the secukinumab arm entered the model in the no response heath state and had secukinumab every week for 4 weeks followed by secukinumab every 4 weeks, up to week 16 (induction phase). For people with no response at week 16 (defined as an HiSCR score of less than 25), the dose was increased to every 2 weeks until week 28 (up-titration phase). People who had a response at week 16 continued with dosing every 4 weeks (maintenance phase). For people whose dose was up-titrated to every 2 weeks, people who had no response at week 28 stopped treatment and instead had BSC. People who had a response at week 28 after up-titration continued to have secukinumab every 2 weeks (maintenance phase). People could transition between HiSCR response states at any time in the model. As with the secukinumab arm, people in the BSC arm of the model entered the model in the no response health state. There was no up-titration phase for BSC, instead everyone entered the maintenance phase at week 16 and could continue to transition between response states. The model used a lifetime time horizon and a

cycle length of 4 weeks. The committee noted several limitations with the company's model structure that are discussed in sections 3.10 to 3.13.

## Up-titration

3.10 In the company's model, people who had no response to secukinumab at week 16 had their dose up-titrated to every 2 weeks (see section 3.9). To model up-titration, the company used transition probabilities based on week 16 to week 28 efficacy data for everyone on the secukinumab every-2-weeks regimen in the SUNNY trials. The EAG noted that the SUNNY trials were not designed to assess up-titration of treatment dosage. In the SUNNY trials, people on secukinumab remained on the dose they were randomised to for the duration of treatment. The EAG was concerned that applying effectiveness based on the full sample randomised to have secukinumab every 2 weeks would likely overestimate effectiveness in the subgroup who had up-titration because of non-response. This is because this subgroup is likely to have HS that is more difficult to treat. So, the EAG preferred not to model up-titration in its base case. The committee noted that the marketing authorisation for secukinumab in HS states that the maintenance dose can be increased based on clinical response. The committee noted that the marketing authorisation does not specify that up-titration should only be offered to people with HS that has not responded. The clinical experts noted that, in clinical practice, they would want to be able to increase the dose from every 4 weeks to every 2 weeks when HS does not respond to dosing every 4 weeks. They added that they would also like to up-titrate the dose in people whose HS has responded, to achieve a better response. The committee also noted that the SUNNY trials did not show a clear dose-response relationship for secukinumab (see section 3.5). The committee considered that it may be appropriate to use up-titration in clinical practice. But, it would like to see more evidence to show a clinical benefit of up-titration in people who do not have a response to the every-4-weeks dose. It concluded that it was inappropriate to include up-titration in the model base case, given that up-titration was not assessed in the SUNNY trials.

## Stopping secukinumab

3.11 In the company's model, response was assessed at week 16 and week 28. At week 16, people who had no response had their dose up-titrated as described in section 3.10. At week 28, secukinumab treatment was stopped for people who continued to have no response. These people transitioned to have BSC. People who had a response at week 16 or week 28 entered the maintenance phase of the model and were assumed to continue secukinumab treatment indefinitely, even if they subsequently lost response. A constant stopping rate from secukinumab to BSC was applied, based on data from the SUNNY trials. The stopping rate is academic in confidence so cannot be reported here. People in the model were assumed to stop treatment at the same rate across all health states. The clinical experts explained that for currently available treatments for HS, they are guided by NICE on how long treatment should be continued for if there is no response. The NICE guidance for adalimumab states that the initial response should be assessed after 12 weeks of treatment, and treatment only continued if there is clear evidence of response (see section 3.3). The summary of product characteristics for adalimumab also recommends that the benefit and risk of continued long-term treatment should be evaluated periodically. The clinical experts agreed that the company's initial assessment of response at 16 weeks is aligned with what generally happens in clinical practice for adalimumab. If adalimumab works initially, then response is assessed every 3 to 6 months after that. If secukinumab was made available, the clinical experts considered that they would add in additional treatments such as antibiotics or surgery if a person's HS stopped responding to secukinumab. If the person's HS continued to not respond to secukinumab, then they would stop treatment. The committee considered that people who had a sustained non-response to secukinumab after the induction phase would likely stop treatment. So, it considered that neither the company nor the EAG's base cases reflected clinical practice, because the no response group in the maintenance phase of the model

remained on treatment indefinitely. The committee considered that it would be reasonable to apply a stopping rule for people who had no response to secukinumab, which would be similar to the stopping rule in place for adalimumab for moderate to severe HS in TA392. But, it considered that it would need further information to determine the most appropriate stopping rule. The committee concluded that it would like to see a scenario where people who lose response in the maintenance phase of the model stop secukinumab and instead have BSC.

### Transition probabilities for BSC arm

3.12 The company used data from the placebo arms of the SUNNY trials to determine transition probabilities for people on BSC between week 0 and week 16. After week 16, the company used week 12 to week 36 data from the PIONEER II study of adalimumab compared with placebo, which informed the cost-effectiveness modelling in NICE's technology appraisal guidance on adalimumab. The company noted that PIONEER II provided data for a longer follow-up period than the SUNNY trials for people who had placebo (36 weeks compared with 16 weeks, respectively). The company considered its approach to be conservative because there are likely to be fewer people who have no response to BSC in PIONEER II (TA392), because this population had not had previous biologicals such as adalimumab. The EAG argued that the company's approach introduced bias because it relied on a naive comparison between treatment arms. The EAG preferred to use data from week 0 to week 16 of the placebo arms of the SUNNY trials for BSC transition probabilities from week 0 to week 16 (induction phase) and also from week 16 onwards (maintenance phase). The EAG noted that although the concomitant treatments allowed in the placebo arms of the SUNNY trials and PIONEER were broadly similar, there are differences in baseline characteristics between the 2 trials. The population in PIONEER II had more severe disease at baseline but were less likely to have had previous surgery and had not had previous treatment with biological therapies. The EAG added that the net effect of these differences is unclear. The

company argued that the EAG's approach lacked face validity, compared with the company's clinically validated approach. The EAG also presented an alternative scenario that assumed people remained in the health state they were in at the last observed time point in the SUNNY trials for the duration of the model (last observation carried forward). The committee considered the BSC response curves for the company's base case, the EAG's base case and the EAG's scenario analysis. The response curves showed the combined proportion of people in the response health state (HiSCR score of 50 to 74) and high response health state (HiSCR score of 75 and over) in the model over 10 years. It noted that the response curve for BSC reached a plateau at 16 weeks in the EAG's scenario analysis, at around 10 months in the EAG's base case and at around 2 years in the company's base case. The point at which the curve plateaued was substantially lower in the company base case than in the EAG base case. The exact figures are considered academic in confidence and cannot be reported here. The clinical experts explained that moderate to severe HS is a progressive disease and so they would expect cohort response rates to decrease over time. So, the committee considered that the plateau in the response rates for the BSC arm of both the company and the EAG base case lacked face validity. The clinical experts added that there was a lack of long-term evidence on the response rates with BSC. So, they were unable to estimate what response rates would be considered most plausible for the BSC arm of the model. The committee considered that it was not appropriate to use the EAG's scenario analysis, which used the last observation carried forward from the SUNNY trials. It considered that it was clinically implausible that people would remain in the same health state that they had been at the end of the trial (week 16 for the placebo arm and week 52 for the secukinumab arm) for the remainder of their lives. The committee noted that the BSC arms of both the SUNNY and PIONEER II studies did not reflect NHS clinical practice (see section 3.7) and this may mean that response to BSC based on both trials could be underestimated. The committee considered that the short

duration in both trials added to the uncertainty in estimating response over the model time horizon. The committee were unable to choose between using the SUNNY or PIONEER II data for BSC, and awaits further information from consultation. But it was concerned that the plateau seen for the BSC arm in both the company and EAG base cases did not reflect clinical practice. To make a decision on the most appropriate source of transition probabilities in BSC, the committee would like to see:

- scenarios where the proportion of people in the response and high response health states decreases over time in the BSC arm
- further validation of the model output with clinical expert input, and compared with additional sources of evidence to support the choice of the best source of data.

## Transition probabilities for secukinumab arm

3.13 As discussed in section 3.5, the SUNNY trials provided 52 weeks of effectiveness evidence for secukinumab. The company derived transition probabilities for the economic model based on data from the secukinumab arms of the SUNNY trials. Data from the overall population of the SUNNY trials was used in the economic modelling (rather than data from the subgroup who had previous biologicals). The company used week 0 to week 16 data from the secukinumab every-4-weeks arms of the SUNNY trials for people in the induction phase. It used week 16 to week 28 data from the every-2-weeks arms for people in the up-titration phase. It used week 16 to week 52 data from the every-2-weeks or every-4-weeks arms of the trials, respectively, for the maintenance phase and remainder of the model time horizon. The committee noted that in both the company and the EAG base cases, the response rates predicted in the secukinumab arm of the model at week 16 overestimated the response rates seen in the SUNNY trials. The exact figures are academic in confidence so cannot be reported here. The committee considered that the initial mismatch between the trial results and model outcomes may have also impacted on the long-term response rates. The committee concluded that it would like

to see a model that reflects the responses seen in the SUNNY trials at week 16 (compared with BSC) and at week 52.

## Utilities

### Health state utility values

3.14 The SUNSHINE and SUNRISE trials collected EQ-5D-3L data between week 2 and week 16. The company used pooled EQ-5D-3L data from both trials and across everyone in the trial to obtain utility values for each HiSCR health state. In its original submission the company applied treatment-specific utilities in all health states. This meant that within the same health state, people on secukinumab had a higher utility than people on BSC. The company revised this assumption at technical engagement stage to include treatment-specific utilities in the no response (HiSCR less than 25) health state only. It used treatment-pooled utility values for all other health states. The company noted that the clinical data from the SUNNY trials showed that for people who had no response, secukinumab showed a statistically significant improvement in disease compared with BSC in terms of:

- percentage change in abscess and inflammatory nodule count from baseline
- percentage of people with no increase in abscesses at week 16
- percentage of people with no increase in draining fistula counts at week 16.

The company also presented data from a repeated measures regression model, with interaction terms for treatment and health state. This showed a statistically significant treatment effect of secukinumab compared with placebo in the no response health state. Based on the evidence presented, the committee considered that it was plausible that secukinumab would improve disease control and quality of life compared with BSC for people who had no response, as classified by HiSCR less than 25 up to week 16. But, it noted that it had not been provided with any

longer-term data to support treatment-specific utility values for the no response health state after week 16. So, the committee considered it appropriate to use treatment-specific utility values for the no response health state up to week 16 only. From week 16 onwards, it preferred to use treatment-pooled utility values for all health states (including the no response health state).

## Costs

### Costs in BSC arm

3.15 As discussed in section 3.12, the company used data from PIONEER II to estimate BSC transition probabilities while the EAG preferred to use data from the SUNNY trials. The trial protocols only allowed concomitant treatment with simple pain management and restricted antibiotic use (see section 3.7). But, the company included costs for a wider range of BSC treatments in its economic model. These included topical and oral antibiotics, dapsone, retinoids, ciclosporin, anti-androgens and surgical procedures. The company stated that BSC treatments are supportive only, and that the company's clinical experts support using data from the placebo arm of the SUNNY trials as a proxy for BSC efficacy in UK clinical practice. The EAG noted that this meant that costs of BSC treatments used in UK practice are included in the company's model but the benefits are not. The EAG noted that the company's approach implicitly assumes that PIONEER II data captures the benefit of these treatments. But the EAG disagreed because the trial does not provide efficacy data for treatments given in UK practice. Given that the efficacy of treatments given in UK practice is unknown, the EAG preferred to use costs based on treatments used in the placebo arm of the SUNNY trials (but still included surgery costs). The EAG also provided a scenario where surgery costs are excluded to align completely with the SUNNY trials. As discussed in section 3.7, the committee concluded that the range of treatments permitted in the SUNNY and PIONEER II trials was more restrictive than that offered to people in UK clinical practice, and this may mean that

response based on both trials would be underestimated. Clinical experts explained that there was a lack of effectiveness data for treatments given in UK clinical practice (section 3.12) and that surgery does not prevent disease progression (section 3.3). The committee considered that, without data on response to treatments given in UK clinical practice, it preferred to align the costs of BSC in the model with the placebo arm of the SUNNY trials.

## Surgery costs

3.16 The company included surgery costs based on the National Schedule of NHS costs (2020/21). It adopted the approach that the EAG in TA392 had used to cost surgery. It assumed that:

- 7% of surgeries were major elective inpatient procedures
- 13% were intermediate elective inpatient procedures
- 13% were intermediate non-elective short-stay procedures
- 67% were intermediate day-case procedures.

This resulted in a weighted average cost for a surgical procedure of £2,402. The EAG preferred to assume that most procedures would be minor and included the cost for minor procedures in its calculation to derive a weighted average cost for a surgical procedure of £1,217. The EAG also did a scenario analysis where surgery costs were excluded. The clinical experts explained that people with moderate to severe HS may have a range of surgery types, from minor non-elective procedures to major elective procedures. They explained that people with acute symptoms are often admitted to the emergency department for small incisions and drainage of abscesses. People may also have narrow excisions as day-case procedures, but these do not alter the disease in surrounding areas. Some people with severe disease opt to have major elective inpatient wide excisions, which are associated with lengthy hospital stays and a long recovery period. But most surgeries are small surgeries, aiming to provide symptomatic relief but with no impact on

preventing disease progression. The clinical experts were unsure whether the company or EAG's estimates were more appropriate. The committee considered that there was uncertainty in the most appropriate surgery costs to include in the model, or whether to include these costs in the model at all. The committee noted that the choice of surgery costs to include in the model had a very limited impact on the cost-effectiveness estimates. It also noted that surgery has little impact on disease progression, but that surgery costs are incurred in UK clinical practice. So, the committee concluded that it was appropriate to include surgery costs in the model because this best reflects NHS clinical practice. Given the uncertainty, the committee conservatively preferred using surgery costs from the EAG base case.

### Hospital resource use rates

3.17 The company used estimates of hospital resource from a survey of 40 UK clinical experts done for TA392. The company did clinical validation of these estimates at technical engagement. It reported that experts broadly agreed with the resource use estimates. The EAG adopted the same resource use frequencies as the company in its model. But, the EAG was concerned that the company's approach lacked transparency, that frequencies were higher than what might be expected in clinical practice, and that uncertainty was not incorporated probabilistically in the economic model. To explore the impact of higher or lower resource use estimates on the incremental cost-effectiveness ratio (ICER), the EAG did exploratory analyses reducing resource use estimates by 25%, 50%, 75% and 100%. The clinical experts noted that the number of surgeries predicted by the company's model seemed high for both arms, but may be plausible given that the estimates also included less intensive surgeries. The clinical experts also added that not all surgeries may be captured because some are done by other specialities. The committee noted the relatively minor impact of the EAG's scenarios on the ICER. The committee concluded that the company's hospital resource use rates were uncertain, but appropriate for use in the model.

### Outpatient visit frequencies

3.18 The EAG was concerned that company's estimates of hospital resource use may double count resource use for outpatient appointments. The company argued that its approach to estimating resource use is aligned with TA392. The committee considered that there was uncertainty in the most appropriate outpatient visit costs to be included in the model, but noted that the impact on the ICER was small. Given the uncertainty, the committee conservatively preferred the use of outpatient visit costs from the EAG base case, which aimed to reduce the possibility of double counting.

## Cost-effectiveness estimates

### Committee's preferred estimates

3.19 The company and EAG base-case deterministic ICERs were £42,415 and £95,821 per QALY gained, respectively. The probabilistic ICERs were £42,268 and £96,353 per QALY gained, respectively.

The EAG preferred to assume that:

- the SUNNY trials data is used for BSC transition probabilities (section 3.12)
- BSC costs are based on treatments used in the placebo arms of SUNNY trials (section 3.15)
- there is no up-titration of secukinumab (section 3.10)
- surgery costs include minor procedures (section 3.16)
- outpatient visits are adjusted to remove potential double counting (section 3.18).

The committee preferred to assume that:

- treatment-specific utility values are applied up to week 16 only (section 3.14)

- BSC treatment costs are aligned with treatments used in the SUNNY trials (section 3.15)
- there is no up-titration of secukinumab (section 3.10)
- secukinumab is stopped for people who have no response in the maintenance phase (section 3.11)
- surgery costs include minor procedures (section 3.16)
- outpatient visits adjusted to remove potential double counting (section 3.18).

The committee could not conclude on a preferred ICER because neither the company nor the EAG's estimates of response over time for people on BSC showed face validity. The committee would like to see:

- A scenario where people who have no response in the maintenance phase of the model stop secukinumab and instead have BSC (section 3.11).
- Scenarios where a declining proportion of people in the response state of the BSC arm is modelled over time (section 3.12).
- Further validation of the model output with clinical expert input, and compared with additional sources of evidence to support the choice of the best source of data (section 3.12).
- A model that reflects the responses seen in the SUNNY trials at week 16 in the secukinumab and placebo arms and at week 52 (section 3.13) in the secukinumab arm
- A model that uses treatment pooled utility values for all health states, including the no response health state from week 16 onwards (section 3.14).

The committee considered that because of the uncertainty around the treatment used in the BSC arm and ongoing response rates for secukinumab and BSC, an acceptable ICER would be at the lower end of the £20,000 to £30,000 per QALY gained threshold range.

# Other factors

## Equality

3.20 The committee considered that the prevalence of HS is higher in women, particularly those of childbearing age, and in people from an African-Caribbean family background. The committee noted that these are protected characteristics under the Equality Act 2010. But because its recommendation does not restrict access to treatment for some people over others, the committee agreed that this was not a potential equality issue.

## Severity

3.21 NICE's health technology evaluations manual notes that when considering overall benefits, the committee can consider decision-making modifiers. The severity modifier allows the committee to give more weight to health benefits in the most severe conditions. The company's absolute and proportional QALY shortfalls were below the cut-offs required for the severity weighting. So, the company did not consider it appropriate to apply a severity modifier. The committee agreed with the company's approach not to include a severity modifier in this population.

## Uncaptured benefits

3.22 The committee did not identify additional benefits of secukinumab that were not captured in the economic modelling. So the committee concluded that all additional benefits of secukinumab had already been taken into account.

# Conclusion

## Recommendation

3.23 Secukinumab is not recommended for treating moderate to severe HS. The trials showed that secukinumab generally improved symptoms of moderate to severe HS compared with placebo. People in the placebo arm of the trial did not have the treatments usually offered to people with

HS in UK clinical practice. So, the benefit of secukinumab is unclear. Also, the trials were both short and it is unclear what response would look like over the longer term. The cost-effectiveness estimates are all above the range NICE considers an acceptable use of NHS resources. So, secukinumab is not recommended.

# 4 Evaluation committee members and NICE project team

## Evaluation 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 being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of each evaluation committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

## Chair

**Baljit Singh**

Vice Chair, technology appraisal committee B

## NICE project team

Each evaluation is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the evaluation), a technical adviser and a project manager.

**Anna Willis**

Technical lead

**Lizzie Walker**

Technical adviser

**Leena Issa**

Project manager

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