NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Final draft guidance

Secukinumab for treating moderate to severe hidradenitis suppurativa

1 Recommendations

1.1 Secukinumab is recommended as an option for treating active moderate to severe hidradenitis suppurativa (acne inversa) in adults when it has not responded well enough to conventional systemic treatment, only if:

- adalimumab is not suitable, did not work or has stopped working
- the company provides secukinumab according to the commercial arrangements (see section 2).

1.2 Assess response to secukinumab after the first 16 weeks of treatment, and only continue if there is clear evidence of a response, defined as:

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

1.3 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 treatment (for example, oral antibiotics) has not worked well

enough is adalimumab. For this evaluation, the company asked for secukinumab to be considered only for people who cannot have adalimumab or whose condition has not responded or has stopped responding to it. This does not include everyone who secukinumab is licensed for.

Evidence from 2 clinical trials shows that secukinumab generally improves symptoms of moderate to severe hidradenitis suppurativa more than placebo in the people the company has asked for it to be considered for.

The most likely cost-effectiveness estimates are within what NICE considers an acceptable use of NHS resources. So, secukinumab is recommended.

2 Information about secukinumab

Marketing authorisation indication

2.1 Secukinumab (Cosentyx, Novartis) is indicated for the treatment of 'active moderate to severe hidradenitis suppurativa (acne inversa) in adults with an inadequate response to conventional systemic HS 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. 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. There is also a complex patient access scheme for secukinumab for hidradenitis suppurativa. This means that the dose given every 2 weeks is supplied to the NHS at a cost equivalent to the dose given every 4 weeks.

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. It is particularly common in people of childbearing age, people with a higher body weight and people who smoke. 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 The clinical experts attending the committee meeting explained that HS is a chronic, inflammatory condition. Some people will have periods in which symptoms may improve or worsen over weeks or months. But, 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. The clinical experts at the committee meeting and the patient expert statement explained that HS has a substantial effect 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. The 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. The clinical experts explained that, if HS is not well controlled with medication, then major surgery may be needed, which has a 3- to 6-month recovery period. Targeting inflammation early with effective treatments can prevent major surgery and scarring. 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 clinical experts added that people with HS have lost faith in medicine because of the lack of treatment options. 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 treatment. 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. The clinical experts explained that people often cycle through multiple courses of tetracycline antibiotics but these rarely control moderate to severe HS. 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 guidance on adalimumab for treating moderate to severe hidradenitis suppurativa (from

now, TA392) recommends adalimumab for moderate to severe HS in adults whose condition has not responded to conventional systemic treatment. The clinical experts explained that almost all people with moderate to severe HS will be offered adalimumab. Adalimumab is contraindicated in some people, 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, there was a clinical response in about half of people 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. The 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 condition does not respond to adalimumab will be offered best supportive care (BSC). The company assumed that BSC includes surgical procedures, antibiotics, retinoids, dapsone, ciclosporin and anti-androgens. The 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 HS is more common in people with a higher body weight. Also,

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 HS 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 used in NHS practice. But it noted that 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 treatment. The company has positioned secukinumab for active moderate to severe HS in people who cannot have 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. The clinical experts noted some limitations with the company's BSC treatments (see section 3.3). They 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 it noted that the clinical data for secukinumab from the pivotal trial was for everyone with active moderate or severe HS, not just people who cannot have adalimumab (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. They compared secukinumab 300 mg subcutaneously every 2 weeks or every 4 weeks with matched placebo in adults with moderate to severe HS. 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 every 2 weeks or every 4 weeks. 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, and 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 with a numerical rating scale of 30 (NRS30; 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% on secukinumab every 4 weeks and 33.7% 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 clinical experts also explained that, in severe HS, it can be difficult to accurately and objectively measure the extent and severity of the condition using HiSCR. This is because it can be challenging to count the number of fistulas in severe HS. 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 have 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 treatment, mostly with adalimumab. The EAG was concerned that the overall population of the SUNNY trials did not match the company's positioning of secukinumab as a second-line biological treatment after adalimumab. The EAG noted that adalimumab and secukinumab have a different mechanism of action. This means that non-response to adalimumab would not necessarily impair the response to secukinumab. But 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 have been greater than that seen in practice. Prespecified subgroup analyses of the SUNNY trial data showed that reaching an HiSCR50 at week 16 was broadly consistent in groups with and without previous exposure to biological treatment. The odds ratio for the every-2-weeks dose was 1.60 for people who had previous biological treatments and 1.64 for people who did not. For the

every-4-weeks dose, it was 1.67 and 1.61 respectively. The committee was initially concerned that there may have been differences between people who had simply had previous adalimumab and people in whom previous adalimumab had not worked. After the committee meeting, the committee noted that most people in the SUNNY trials who had previous biological treatments 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, it concluded that the results of the full trial population (that is, people who had and had not had biological treatments) were generalisable to the company's narrower target population. This was people with moderate to severe HS not able to have adalimumab, including people 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 other medication alongside secukinumab or placebo. The trial protocols allowed simple pain management and restricted use of antibiotics as concomitant treatments. But the clinical experts noted the broad range of treatment options that are offered to people with HS in UK clinical practice, including surgery (see section 3.3). They added that the evidence base for treatments typically used for 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 was possible that people having the BSC treatments permitted in the SUNNY trials had worse efficacy outcomes than people having BSC in UK clinical practice. This may have favoured 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 every 2 weeks or every 4 weeks. 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 for the long-term effectiveness of secukinumab. The EAG noted that the follow-up duration of the SUNNY trials was short. The company submission and 1 clinical expert at the first committee meeting also stated that, because HS is a progressive condition, it would have been 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 TA392. 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)
- death.

People in the secukinumab arm entered the model in the no-response health state. They then 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. At the first committee meeting, 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 in clinical practice this subgroup would be likely to have HS that is more difficult to treat. So, because of the lack of clinical efficacy data in this group of people, the EAG preferred not to model up-titration in its base case. At the first committee meeting, the committee noted that the marketing authorisation for secukinumab in HS states that the maintenance dose can be increased based on clinical

response. But the committee concluded that 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. In response to the draft guidance consultation, the company noted that having the flexibility to up-titrate secukinumab is important given the absence of other treatment options. At the second committee meeting, 1 clinical expert noted that the marketing authorisation for secukinumab in adults with plaque psoriasis allows for up-titration in people with a body weight of 90 kg or higher. The clinical experts considered that it may be beneficial to up-titrate secukinumab in people with HS with a high body weight or with more severe HS. But this was providing that there were no safety concerns with using the higher dose. They noted that there is uncertainty in how up-titration would be applied in NHS practice, but considered that a potential approach may be:

- at week 16 (end of the induction phase), to stop secukinumab for people with HS that does not respond to secukinumab (HiSCR score of less than 25)
- at week 16 (end of the induction phase), to up-titrate secukinumab from the every-4-weeks dose to the every-2-weeks dose for people with HS that partially responds to it (HiSCR score of 25 to 50)
- after week 16 (maintenance phase), to up-titrate secukinumab from the every-4-weeks dose to the every-2-weeks dose for people with HS that initially responded to it at week 16 (HiSCR score of greater than 25) then stopped responding for a consecutive period of 12 weeks (HiSCR score of less than 25), then to stop secukinumab if the person's HS did not respond after 12 weeks of the up-titrated dose.

The committee noted that, in the company's model:

- at week 16 (end of the induction phase), secukinumab would be up titrated from the every-4-weeks dose to the every-2-weeks dose for people with HS that does not respond to it (HiSCR score of less than 25)

- after week 16 (maintenance phase), secukinumab would be stopped for people with HS that initially responded to it at week 16 (HiSCR score of greater than 25), then stopped responding for a consecutive period of 12 weeks (HiSCR score of less than 25).

The committee noted that the approach to modelling up-titration applied in the company's model may not reflect how clinicians will carry out up-titration in clinical practice. The committee also noted that the marketing authorisation for secukinumab states that 'clinical response is usually achieved within 16 weeks of treatment. Consideration should be given to discontinuing treatment in patients who have shown no response by 16 weeks of treatment. Some patients with an initial partial response may subsequently improve with continued treatment beyond 16 weeks.' The committee also agreed with the EAG that there was no evidence to support up-titration available from the SUNNY trials. It also agreed that applying effectiveness based on the full sample randomised to have secukinumab every 2 weeks was likely to overestimate the benefit of up-titration. The committee noted that the SUNNY trials did not show a clear dose-response relationship for secukinumab (see section 3.5). So, it considered that there was substantial uncertainty in the application of up-titration in the company's model. But, the committee noted that there is a complex patient access scheme for secukinumab in hidradenitis suppurative. This means that the dose given every 2 weeks is supplied to the NHS at a cost equivalent to the dose given every 4 weeks. The committee concluded that it was not possible to robustly model the inclusion of up-titration in the model. So, it preferred to remove up-titration in the base case. The committee noted the comments from the clinical experts that there may be some people who would benefit from up-titration in clinical practice, and that it is included in the marketing authorisation. So, it considered that there is uncertainty around up-titration in clinical practice.

Stopping secukinumab

3.11 In the company's model at the first committee meeting, response was assessed at week 16. At week 16, people who had no response had their dose up titrated (as described in section 3.10) and response was assessed again at week 28. 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. Separate stopping rates for year 1 and for year 2 onwards were applied, based on data from the SUNNY trials. People in the model were assumed to stop treatment at the same rate across all health states. The clinical experts at the first committee meeting 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. TA392 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 to secukinumab 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 to be 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. At the first meeting, the committee considered that people whose HS had a sustained non-response to secukinumab after the induction phase would likely stop treatment. So, it considered that neither the company's 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. At the second meeting, the company's base case included the following stopping rules, which were broadly aligned with the stopping rules used in TA392:

- Secukinumab is stopped in people in the no-response health state at the end of the induction phase (week 16 in the scenario in which up-titration was not allowed or week 28 in the scenario in which up-titration was allowed).
- Secukinumab is stopped in people whose HS stops responding to secukinumab in the maintenance phase and non-response is maintained for 12 weeks (this was applied in the model using tunnel states to track when people entered the no-response health state).

The EAG was satisfied that the company's stopping rules had been implemented correctly in the model. The clinical experts agreed that they would want to stop secukinumab if it was not effective. So, it was reasonable to stop secukinumab if there was no response at the end of induction or after 12 weeks of no response during maintenance. For the scenario in which up-titration was modelled, see section 3.10. The committee concluded that the company's revised model incorporating stopping rules for secukinumab in both the initiation and maintenance phases was appropriate.

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 2 study of adalimumab compared with placebo, which informed the cost-effectiveness modelling in TA392. The company noted that PIONEER 2 provided data for a longer follow-up period (36 weeks) than the SUNNY trials (16 weeks) for people who had placebo. The company considered its approach to be conservative because there were

likely to have been fewer people whose HS did not respond to BSC in PIONEER 2. This was because this population had not had previous biological treatments 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 2 were broadly similar, there were differences in baseline characteristics between the 2 trials. The people in PIONEER 2 had more severe HS at baseline. But they 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 was unclear. The response curves presented at the first committee meeting 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. The response curve for BSC reached a plateau 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's base case than in the EAG's 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 condition, 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 committee also noted that the BSC arms of both the SUNNY and PIONEER 2 studies did not reflect NHS clinical practice (see section 3.7). So, response to BSC in the model could underestimate response to BSC in clinical practice. During the draft guidance consultation period, the company carried out clinical validation with 7 clinical experts, all of whom agreed that it was reasonable to use data

from the placebo arm from PIONEER 2 as proxy for the placebo arm in the SUNNY trials. All of the experts considered that the EAG's response curves lacked face validity. They also thought that the predicted high response rates underestimated the unmet need in the moderate to severe HS population who had previously had biological treatment. The company added that its approach was more closely aligned with the model predictions and the overall discounted quality-adjusted life year (QALY) gain in TA392 than the EAG's approach. The EAG highlighted that the company's approach implies that secukinumab has an increasing treatment effect over time, with no evidence to support this. The EAG also agreed with the committee's previous conclusion that response rates for the placebo arm in the SUNNY trials may have underestimated response in clinical practice because the treatments permitted in the SUNNY trials were more restrictive (see section 3.7). The company also provided scenarios assuming a decreasing proportion of responders over time. But the EAG was concerned that arbitrarily reducing proportion responding to BSC over time would increase uncertainty. The clinical experts at the second meeting considered the response curves presented in light of the additional validation done by the company. They agreed that the EAG's curve predicted response rates for BSC that were too high and did not reflect clinical experience. The committee considered that the EAG's response curve for BSC may not be reflective of response rates for BSC in clinical practice and the company's estimates of BSC response may be more plausible. The committee noted that the company's approach, based on PIONEER 2 data, resulted in outcomes that were more closely aligned with TA392. This is expected because TA392 also used PIONEER 2 data. The committee noted that the relative difference between the secukinumab and BSC response curves was a driver of cost-effectiveness, rather than the absolute response rates. The committee noted that the relative difference between response curves based on the EAG's approach was more closely aligned with clinical-effectiveness outcomes from the SUNNY trials at week 16. But the committee noted that response rates for people on secukinumab in the SUNNY trials

increased between weeks 16 and 52. The committee noted that there was substantial uncertainty about the long-term benefits of secukinumab because of the lack of comparative data from the SUNNY trials after week 16. The committee concluded that the long-term response rates were highly uncertain, but it preferred using transition probabilities from the placebo arm of PIONEER 2 because they better reflected clinical practice.

Transition probabilities for secukinumab arm

3.13 As discussed in section 3.5, the SUNNY trials provided 52 weeks of clinical-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 biological treatments (see section 3.6). 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. For people who did not have up-titration, it used week 16 to week 52 data from the every-4-weeks arm for the maintenance phase and for the remainder of the model time horizon. For people who had up-titration, it used week 16 to week 52 data from the every-2-weeks arm for the maintenance phase and for the remainder of the model time horizon. The committee noted that, in both the company's and EAG's 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 affected the long-term response rates. In response to the draft guidance consultation, the company explained that the initial mismatch was because of the method used to estimate transition probabilities. The model used transition probabilities averaged across multiple model cycles. This was

because it had a smoothing effect, which reduced the effect of random fluctuations. In response to consultation, the company revised its approach to use per-cycle transition probabilities for the induction phase, while maintaining average transition probabilities beyond week 16. During the second meeting, the committee noted that the revised response curves still overestimated response compared with the response rates for the full analysis set reported in the company's original submission or the trial publication (see section 3.5). The company's modelled response rate is academic in confidence so cannot be reported here. After the meeting, the company explained that the discrepancy between the model predictions and the observed response rate was because transition probabilities in the model were informed by the population without missing data. The committee noted that the placebo response rate was also higher in the population without missing data compared with the full analysis set, but the difference was smaller than in the secukinumab arms. The committee's preference was to align the model with response rates from the full analysis set. It concluded that the company's model may have overestimated the initial benefit of secukinumab. This will bias the cost-effectiveness results in favour of secukinumab, though the size of the effect is uncertain.

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 for 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 score of 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 HS compared with BSC from week 2 to week 16 for:

- percentage change in abscess and inflammatory nodule count
- the percentage of people with no increase in abscesses
- the percentage of people with no increase in draining fistula counts.

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 for 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 control of HS and a person's quality of life compared with BSC for people with an HiSCR score of 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. In response to the draft guidance consultation, the company stated that longer-term data collection was not feasible. This was because it would have been unethical to keep people in the trial on placebo for longer than 16 weeks. But data from the placebo arm of PIONEER 2 showed that utility decreased between week 12 and week 36, suggesting that quality of life on placebo deteriorated over time. This was in contrast to data from the secukinumab arm of the SUNNY trials, which showed that clinical benefit and quality of life were maintained to week 52. This was across all response categories, including people with an HiSCR score of less than 25. The EAG agreed with the company that using treatment-specific utility values in the no-response health state was justified. The EAG noted that a stopping rule is now applied for people whose condition does not respond to secukinumab (see section 3.11). So, it thought that the risk of people whose condition consistently does not respond getting a utility gain in the no-response health state was minimised because these people would now transition to BSC. During the second meeting, the committee remained concerned that the company's

base case assumed a utility benefit for people on secukinumab in the no-response health state for the entire model time horizon, with limited evidence to support this. 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 2 to estimate BSC transition probabilities. 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 and anti-androgens. The company stated that BSC treatments are only supportive. It also said that its clinical experts supported 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 were included in the company's model but the benefits were not. The EAG noted that the company's approach implicitly assumed that PIONEER 2 data captured the benefit of these treatments. But the EAG disagreed because the trial did not provide efficacy data for treatments used in UK practice. Given that the efficacy of treatments used in UK practice is unknown, the EAG preferred to use costs based on treatments used in the placebo arm of the SUNNY trials. As discussed in section 3.7, the committee concluded that the range of treatments permitted in the SUNNY and PIONEER 2 trials was more restrictive than that offered to people in UK clinical practice. This may mean that response based on both trials was underestimated. The clinical experts explained that there was a lack of effectiveness data for treatments used in UK clinical practice

(see section 3.12). The committee considered that, without data on response to treatments used in UK clinical practice, it preferred to align the costs of BSC in the model with the placebo arm of the SUNNY trials. In response to the draft guidance consultation, the company updated its base case to align with the committee's preference. The committee concluded that it was satisfied with the company's updated approach.

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 skin procedures
- 13% were intermediate elective inpatient skin procedures
- 13% were intermediate non-elective short-stay skin procedures
- 67% were intermediate day-case skin procedures.

This resulted in a weighted average cost for a surgical procedure of £2,402. The EAG preferred to weight according to finished consultant episodes across all grades of skin procedure (including minor) and across day-case and elective inpatient settings. The EAG's weighted average cost for a surgical procedure was £1,217. The EAG also did a scenario analysis in which surgery costs were excluded because surgery was not permitted in the SUNNY trials. During the first committee meeting, 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 HS in surrounding areas. Some people with severe HS 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 effect on

preventing disease progression. In response to the draft guidance consultation, the company provided a scenario in which it assumed that, for day-case procedures, 33.5% would be intermediate and 33.5% would be minor, rather than all day-case procedures being intermediate grade. In the second meeting, 1 clinical expert highlighted that there is substantial regional variation in the types of surgeries people with HS have. The clinical experts considered that the most appropriate approach was uncertain. But they agreed that, of all the options presented, the company's scenario appeared to be the best reflection of the split of surgery types offered in clinical practice. The committee noted that surgery has little effect on disease progression, but that surgery costs are incurred in clinical practice. So, the committee concluded that it was appropriate to include surgery costs in the model. It considered that there was uncertainty about the preferred approach to costing surgery. But it preferred to align with the company's scenario analysis, based on the feedback received from the clinical experts.

Hospital resource-use rates

3.17 The company used estimates of hospital resource use from a survey of 40 UK clinical experts done for TA392. The company clinically validated 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
- included frequencies that were higher than what might be expected in clinical practice
- did not incorporate uncertainty 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 they thought this may be plausible, given that the estimates also included less intensive surgeries. The clinical experts also added that not all surgeries may have been captured because some are done by other specialities. The committee noted the relatively minor effect 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 the company's estimates of hospital resource (see section 3.17) use may have double counted resource use for outpatient appointments. The company argued that its approach to estimating resource use was aligned with TA392. In response to the draft guidance consultation, the company provided additional reassurance that outpatient resource use was not double counted. This included full details of the exact questions posed to the clinical experts consulted for TA392. Given the additional information provided, the EAG were satisfied that the risk of double counting was low. It accepted the company's preferred outpatient resource-use estimates. The committee agreed with the company's and EAG's preferred assumptions. But it noted the remaining uncertainty around hospital resource-use rates in general (see section 3.17).

Cost-effectiveness estimates

Committee's preferred estimates

3.19 The company's base-case deterministic ICER was £10,504 per QALY gained and the EAG's was £31,073 per QALY gained. The company's probabilistic ICER was £10,411 per QALY gained and the EAG's was £31,055 per QALY gained. The differences between the company's and EAG's base case were that the EAG preferred to assume that:

- up-titration should not be modelled (see section 3.10)

- BSC transition probabilities should be based on SUNNY trial data (see section 3.12)
- surgery costs should include mainly minor procedures (see section 3.16).

The committee preferred to assume that:

- up-titration should not be modelled (see section 3.10)
- secukinumab should be stopped for people with HS that does not respond at week 16 and for people with HS that loses response after week 16 and has maintained no response for 12 weeks (see section 3.11)
- transition probabilities for BSC should be sourced from the week-12 to week-36 data from the placebo arm of PIONEER 2 (see section 3.12)
- treatment-specific utility values should be used for the no-response health state up to week 16 only; from week 16 onwards, treatment-pooled utility values are preferred for all health states (see section 3.14)
- BSC costs should be aligned with treatments used in the SUNNY trials (see section 3.15)
- the approach used in company's scenario analysis is appropriate for costing surgery (see section 3.16)
- the company's estimates of hospital resource use are appropriate (see section 3.17)
- the company's and EAG's estimates of outpatient visit frequencies are appropriate (see section 3.18).

The committee highlighted several areas of substantial uncertainty including that:

- the SUNNY trials may not be generalisable to the decision problem because most people in the trials had not had biological treatment (see section 3.6)
- the BSC treatments in the SUNNY trials are not reflective of treatments that people are likely to have in clinical practice (see section 3.7)

- there is a lack of comparative data from the SUNNY trials after week 16, which leads to uncertainty in appropriate longer-term response rates (see section 3.8 and section 3.12)
- modelled response rates for secukinumab and placebo do not reflect the full analysis set of the SUNNY trials (see section 3.13)
- the committee's preferred model excludes up-titration because this cannot be modelled robustly (see section 3.10)
- the most appropriate costs for surgery are uncertain (see section 3.16)
- the most appropriate hospital resource-use rates are uncertain (see section 3.17).

The committee's preferred deterministic ICER was £18,439 per QALY gained and probabilistic ICER was £18,099 per QALY gained. Because of the high level of uncertainty in the clinical and economic evidence, the committee agreed that an acceptable ICER would be around £20,000 per QALY gained.

Other factors

Equality

3.20 The committee considered that the prevalence of HS is higher in women and in Black African and Caribbean ethnicities. The committee noted that these are protected characteristics under the Equality Act 2010. But, because its recommendations do 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 needed 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 The trials showed that secukinumab generally improved symptoms of moderate to severe HS compared with placebo. The most likely cost-effectiveness estimates are within what NICE considers an acceptable use of NHS resources. So, secukinumab is recommended.

4 Implementation

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 integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation within 3 months of its date of publication.

4.1 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal guidance 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 draft guidance.

4.2 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 hidradenitis suppurativa and the doctor responsible for their care thinks that secukinumab is the right treatment, it should be available for use, in line with NICE's recommendations.

5 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 and Vonda Murray

Project manager

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