Secukinumab for treating moderate to severe hidradenitis suppurativa

Slides for public, redacted

Technology appraisal committee B [07 June 2023]

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Company: Novartis

Background on hidradenitis suppurativa (HS)

Condition

- Hidradenitis suppurativa (HS) is a painful, long-term skin condition that causes abscesses and scarring[1]
- The exact cause of HS is unknown but it occurs in skin folds where there are sweat glands, in particular the groin and armpits

Epidemiology

- Affects about 1 in 100 people and is more common in women than men[1]

Symptoms and prognosis

- Symptoms of HS can range from mild to severe:
    - Early symptoms include isolated, painful nodules; with or without intermittent inflammation
    - Disease progression is characterised by development of sinus tracts (pus-discharging tunnels) fistulas and/or abscesses
- Extent and severity of disease are often assessed using the Hurley staging system
- The focus of the company's submission is moderate (Hurley stage II) to severe (Hurley stage III) HS

Abbreviations: HS, hidradenitis suppurativa

Clinical perspectives

Submission received from the British Association of Dermatologists

- Scarring due to HS limits function and reduces the ability to work and study
- Reversal of scarring may require extensive surgery
- So preventing progression of HS is important
- Alternatives to adalimumab are needed for people where treatment has failed to work, or for people with contraindications

"Many patients on adalimumab therapy still experience substantial morbidity. In addition, secondary failure of adalimumab often occurs"

"Adalimumab and other anti-TNF-alpha drugs are contraindicated in those with a personal or family history of demyelinating diseases such as multiple sclerosis, so secukinumab [could provide] a potential option is this group."

Clinical experts: How does HS typically progress over time?

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Abbreviations: HS, hidradenitis suppurativa; TNF, tumour necrosis factor

Patient perspectives

Submission from patient expert

- HS has a substantial impact on quality of life
  - Challenges include pain and intense itching, and living with chronic, inflamed and draining wounds
  - People with HS often experience anxiety and depression

- There is a stigma around HS and a culture of patient blame from some healthcare professionals
  - Average time to diagnosis of 7 to 10 years

- Financial burden on people with HS and family members
  - Some people cannot work with HS
  - High household bills from washing of clothes/bed linen or cost of prescriptions, parking or transport for appointments

- Surgical intervention can be helpful but is limited to a specific area and time off work is required to heal post-surgery
- Biologics reduce pain and level of inflammation for some people, but do not work in others

"Living with moderate to severe HS is incredibly difficult and can be described as relentless. Many long-standing HS sufferers will say it has destroyed relationships the chance of being a parent, getting married [and] their career"

"The unpredictability means we can feel unreliable, we pull out of social plans, we let people down or we recluse and don't engage in activity as we are tired of disappointing people"

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Abbreviations: HS, hidradenitis suppurativa

Equality considerations

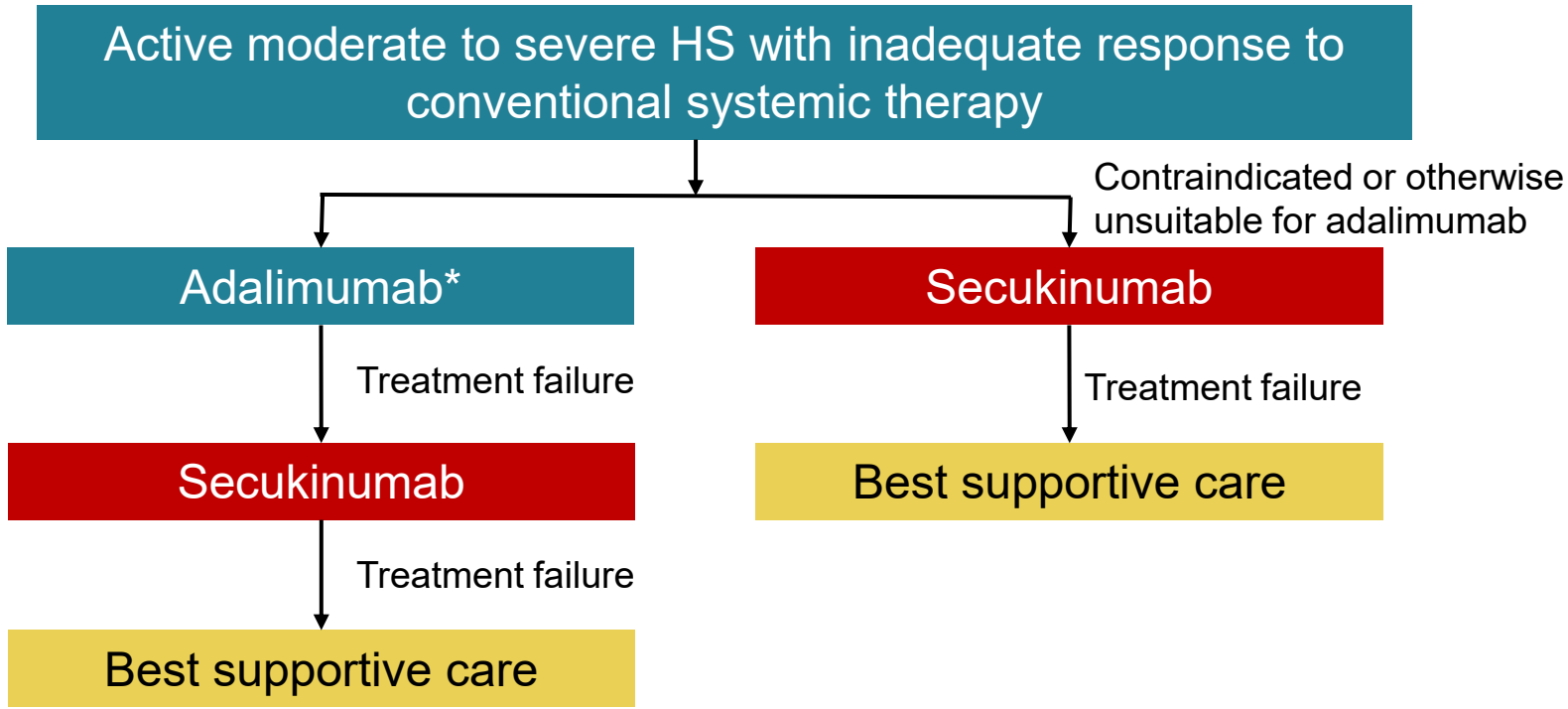
- The incidence of HS is higher in people of African-Caribbean family background as compared with people of European family background
- Peak prevalence is in females of childbearing age

Abbreviations: HS, hidradenitis suppurativa

Treatment pathway

Company's proposed positioning of secukinumab in the treatment pathway

Figure 1: Company's proposed positioning of secukinumab in the treatment pathway



Does the clinical pathway reflect NHS clinical practice?
What is best supportive care in NHS clinical practice?
What proportion of people would be contraindicated to adalimumab?

Conventional systemic therapy[1]:

- Oral tetracyclines
- Oral clindamycin and rifampicin for those unresponsive to oral tetracyclines
- Acitretin or dapsone considered in people unresponsive to earlier antibiotics

Adalimumab is recommended for moderate to severe HS in adults whose disease has not responded to conventional systemic therapy (TA392)

Contraindications to adalimumab:

- Hypersensitivity to active substance
- Active TB or other severe infections
- Moderate to severe heart failure

Best supportive care:

- Surgical procedures, antibiotics, retinoids, dapsone, ciclosporin and anti-androgens

Abbreviations: HS, hidradenitis suppurativa; TB, tuberculosis.

Secukinumab (Cosentyx, Novartis)

Marketing authorisation	• Secukinumab has an EU marketing authorisation for the treatment of "active moderate to severe hidradenitis suppurativa (acne inversa) in adults with an inadequate response to conventional systemic hidradenitis suppurativa therapy".
Mechanism of action	• Fully human IgG1/κ monoclonal antibody, which targets IL-17A, inhibiting its interaction with the IL-17 receptor • This inhibits the release of proinflammatory cytokines, chemokines and mediators of tissue damage
Administration	• Secukinumab 300 mg is self-administered by subcutaneous injection, with initial weekly dosing from week 0 to 4, followed by maintenance dosing every 4 weeks with the possibility to up-titrate to every 2 weeks
Price	• List price per 300 mg pre-filled pen: £1,218.78 • There is a commercial arrangement (simple PAS) already in place for secukinumab across all indications

Abbreviations: CHMP, Committee for Medicinal Products for Human Use; MHRA, Medicines and Healthcare Products Regulatory Agency; PAS, patient access scheme.

Decision problem

	Final scope	Company
Population	Adults with moderate to severe HS	Adults with **active** moderate to severe HS **for whom adalimumab is contraindicated or otherwise unsuitable, including those who have failed to respond or have lost response to prior adalimumab treatment –** secukinumab is not anticipated to be cost-effective in the full population, given the availability of biosimilar adalimumab
Intervention	Secukinumab	As per scope
Comparators	Adalimumab, best supportive care	Best supportive care **only**
Outcomes	Disease severity, disease progression, clinical response, inflammation and fibrosis, discomfort and pain, adverse effects, HRQL	As per scope
Subgroups	People with no response to prior adalimumab treatment	As per scope

EAG comments:

- Company has positioned secukinumab as a second-line treatment following biologics such as adalimumab. EAG has some concerns about the omission of adalimumab as a comparator.
- Agrees that infliximab is not established clinical practice

Abbreviations: HRQL, health-related quality of life; HS, hidradenitis suppurativa

Issues

Key issues	Resolved?	ICER impact
BSC transition probabilities *Should the transition probabilities for BSC be taken from week 12-36 data of PIONEER II, week 0-16 of the SUNNY trials, or be based on the last observation carried forward from the SUNNY trials?*	No	Large
Alignment of costs and benefits for BSC *Should the costs for the BSC arm of the model be aligned with the placebo arm of the SUNNY trials or with clinical expert opinion on UK clinical practice?*	No	Unknown
Hospital resource use rates *Has the uncertainty around hospital resource use rates been adequately captured?*	No	Unknown
Health state utility values *What are the most appropriate utility values: treatment specific, treatment pooled or treatment specific for the non-response health-state only?*	Yes	Large
Other issues		
Inclusion of up-titration from Q4W to Q2W dose	No	Small
Surgery costs	No	Small
Outpatient visits costs	No	Small

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Abbreviations: BSC, best supportive care; ICER, incremental cost-effectiveness ratio; QxW, every x weeks.

Clinical effectiveness

NICE National Institute for Health and Care Excellence

Key clinical trials

Company's clinical effectiveness evidence comes from two identically designed phase 3 trials – SUNSHINE and SUNRISE (known collectively as the SUNNY trials)

	SUNSHINE (n=541) and SUNRISE (n=543)
Design	Phase 3 randomised, double-blind, placebo-controlled, parallel-group trials
Population	Adults (≥18 years old) with moderate to severe HS
Intervention	Secukinumab 300mg subcutaneous injection Q2W or Q4W
Comparator(s)	Placebo subcutaneous injection Q2W or Q4W
Duration	52 weeks, comparative evidence available for 16 weeks only
Primary outcome	Proportion of patients with an HS clinical response score of 50 (HiSCR50) at week 16, defined as a ≥50% decrease in abscess and inflammatory nodule (AN) count with no increase in the number of abscesses and/or draining fistulae
Key secondary outcomes	AN count, HS flares, NRS30 (skin pain); at week 16
Locations	Worldwide: 132 study sites, 12 sites in UK (n= 46, across both trials)
Used in model?	Yes (HiSCR50, EQ-5D-3L, adverse events), data naïvely pooled due to identical study design

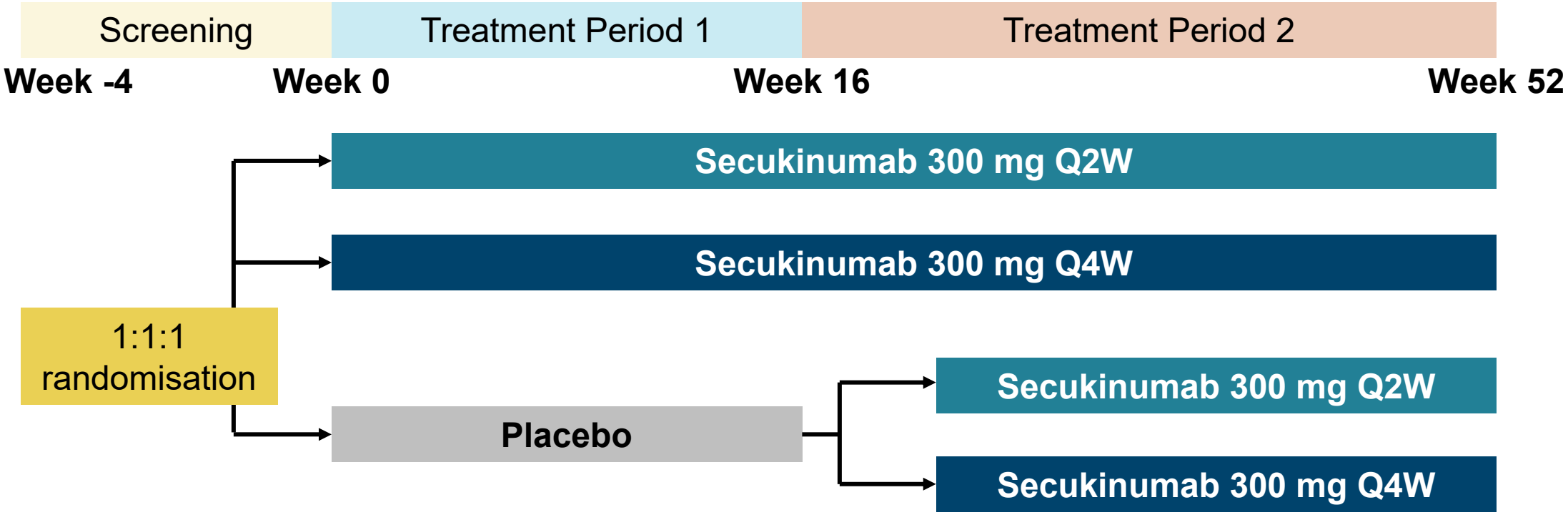
Abbreviations: AN, abscess and inflammatory nodule; EQ-5D-3L, EuroQol 5 Dimensions 3 Levels; HiSCR50, HS clinical response score of 50; HS, hidradenitis suppurativa; QxW, every x weeks; NRS, numerical rating scale.

SUNNY trial design

People in SUNNY were randomised to secukinumab Q2W or Q4W, or placebo

- Comparative clinical effectiveness data available up to Week 16 only
- Anticipated marketing authorisation is for maintenance dosing Q4W with the possibility to up-titrate to Q2W
- SUNNY trials did not specifically assess the clinical effectiveness of up-titration

Figure 1: SUNNY trial design



Abbreviations: HS, hidradenitis suppurativa; QxW, every x weeks

SUNNY trials: Results

Proportion of people with HiSCR50 at week 16 was greater for secukinumab versus placebo. Difference was statistically significant across both trials and doses, except for the Q4W dose in SUNSHINE

Table 1: SUNNY trial results, primary outcome, week 16

Study	PBO	SEC Q2W			SEC Q4W		
	% response	% response	OR vs PBO (95% CI)	p-value*	% response	OR vs PBO (95% CI)	p-value*
SUNSHINE	33.7	45.0	1.75 (1.12, 2.73)	p=0.0070**	41.8	1.48 (0.95, 2.32)	p=0.0418 (not statistically significant)
SUNRISE	31.2	42.3	1.64 (1.05, 2.55)	p=0.0149**	46.1	1.90 (1.22, 2.96)	p=0.0022**

Secondary outcomes:

- Greater reduction in skin pain (NR30), greater decrease in abscess and inflammatory nodule count and fewer people experiencing HS flares at week 16 for secukinumab versus placebo
- Mixture of statistically significant and non-statistically significant results across Q4W and Q2W treatment arms and trials

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Abbreviations: HiSCR50, hidradenitis suppurativa clinical response score of 50. **Notes** *one-sided p value; **statistically significant based on the pre-defined testing hierarchy.

Generalisability of SUNNY trials to decision problem

Background

Relevance for population in whom adalimumab is unsuitable

- ~23% of participants in SUNNY trials had previously received systemic biologic therapy, mostly adalimumab
- Pre-specified subgroup analyses of SUNNY trials show that achievement of HiSCR50 was broadly consistent in groups with and without previous exposure to biologics (see **Figure 1**, next slide)
- Company model uses data from full SUNNY population (biologic-experienced and biologic-naïve)

Generalisability of BSC arm

- SUNNY trial protocols restricted concomitant medication (BSC) to simple pain management and restricted use of antibiotics, but excluded retinoids, other biologics, ciclosporin, dapsone or anti-androgens

EAG comments:

- Overall population of SUNNY trials does not match company's positioning of secukinumab as second-line after biologics
- Adalimumab and secukinumab use a different mechanism of action, so non-response to adalimumab would not impair the response to secukinumab
- However, secukinumab is likely to be used in more difficult to treat cases that are unresponsive to adalimumab, which may have increased the effect size in favour of secukinumab
- BSC treatments in SUNNY may not align with NHS clinical practice

Are the SUNNY trials appropriate for the decision problem?

Abbreviations: BSC, best supportive care

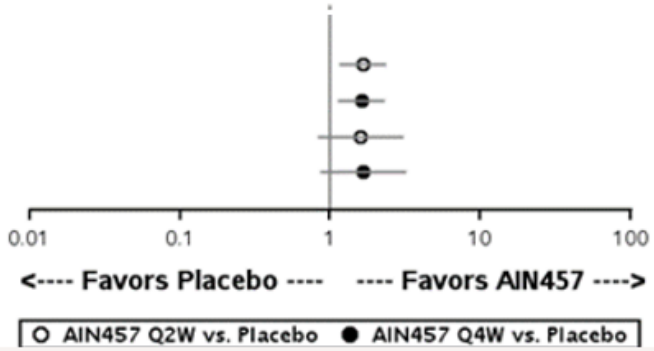
Subgroup analysis

Pre-specified subgroup analysis based on previous exposure to biologics shows similar odds ratios across biologic-experienced and biologic-naïve subgroups

Company

Figure 1: Subgroup analysis of primary outcome based on previous exposure to biologics (pooled analysis of SUNNY trials)

Subgroup	Treatment Comparison	OR (95% CI)	P-value	Placebo (n*/m, %)	AIN457 (n*/m,%)
Previous exposure to biologics					
N	AIN457 Q2W vs. Placebo	1.64 (1.15, 2.33)	0.0065	92.0/269 (34.2)	128.1/281 (45.6)
	AIN457 Q4W vs. Placebo	1.61 (1.13, 2.29)	0.0087	92.0/269 (34.2)	126.8/279 (45.4)
Y	AIN457 Q2W vs. Placebo	1.60 (0.83, 3.08)	0.1604	25.7/ 94 (27.3)	29.6/ 80 (37.0)
	AIN457 Q4W vs. Placebo	1.67 (0.86, 3.22)	0.1281	25.7/ 94 (27.3)	31.4/ 81 (38.8)



Notes: Nominal significance was not achieved in the biologic-experienced subgroup due to the smaller sample size as compared with biologic-naïve patients. **Abbreviations:** AIN457, secukinumab; BSC, best supportive care; CI, confidence interval; OR, odds ratio; QxW, every x weeks.

Cost effectiveness

NICE National Institute for Health and Care Excellence

Company's model structure

Company

- Developed a Markov model with 5 health states based on HiSCR, in line with the model used in TA392. Model health states included:
  - **Non-response:** HiSCR: <25
  - **Partial response:** HiSCR: 25–49
  - **Response:** HiSCR: 50–74
  - **High response:** HiSCR: ≥75
  - **Death**

Table 1: Company's model features

Perspective	NHS/PSS
Time horizon	Lifetime
Cycle length	4 weeks
Discounting (costs and effects)	3.5% annually

- The secukinumab arm of the model included an induction phase (week 0-16), an up-titration phase (week 16-28) for non-responders at week 16, and a maintenance phase (week 16/28 onwards)
- The BSC arm of the model included induction and maintenance phases only
- Model features are presented in **Table 1** and the model structure diagram is presented on the next slide

EAG comments:

- Model structure is appropriate

Abbreviations: BSC, best supportive care; HiSCR, hidradenitis suppurativa clinical response; PSS, personal and social services.

Company's Markov model – secukinumab arm

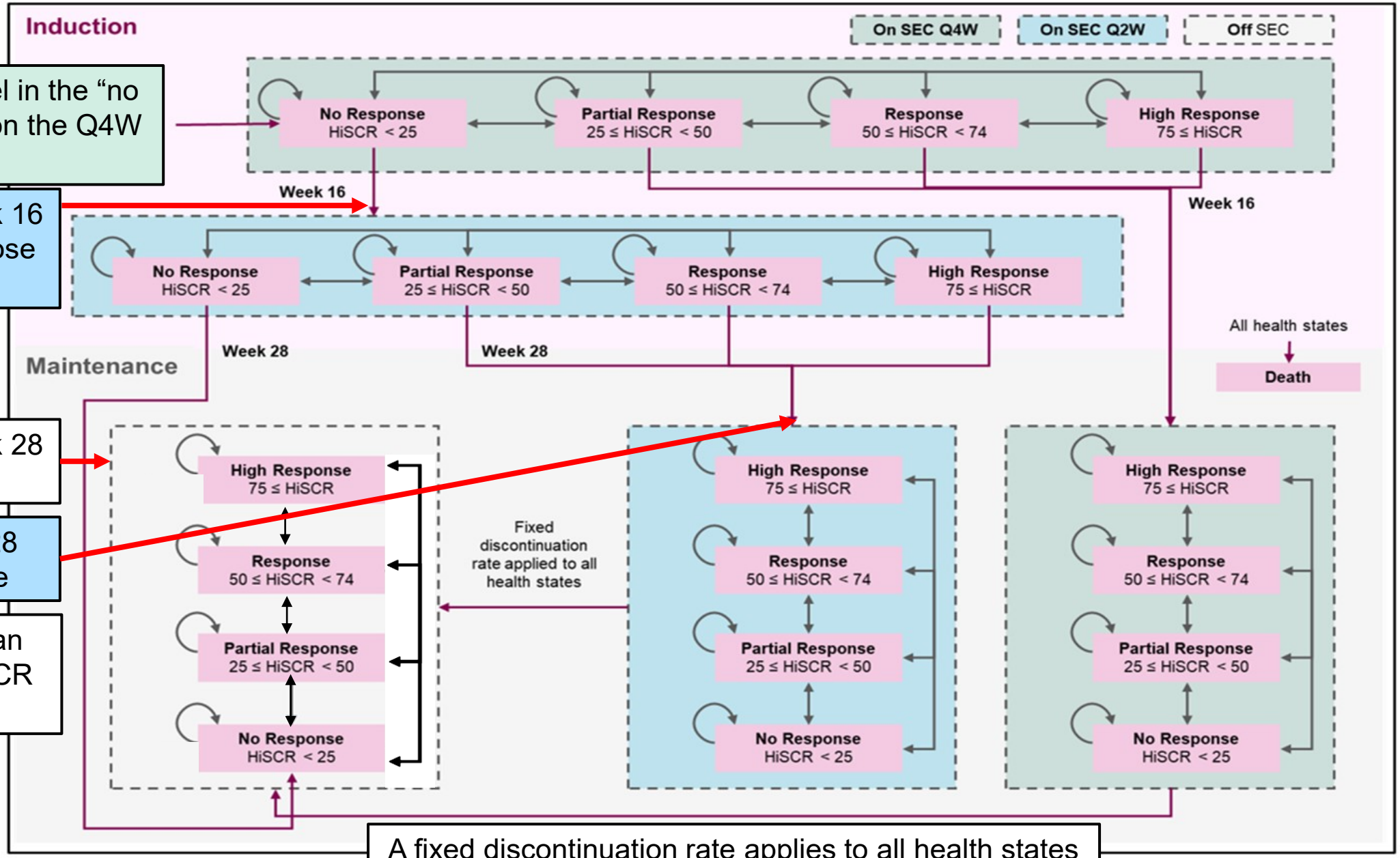
Patients enter the model in the "no response" health state on the Q4W dose

Non-responders at week 16 up-titrate to the Q2W dose until week 28

Non-responders at week 28 stop treatment

Responders at week 28 stay on the Q2W dose

Patients in all states can transition between HiSCR response states



A fixed discontinuation rate applies to all health states

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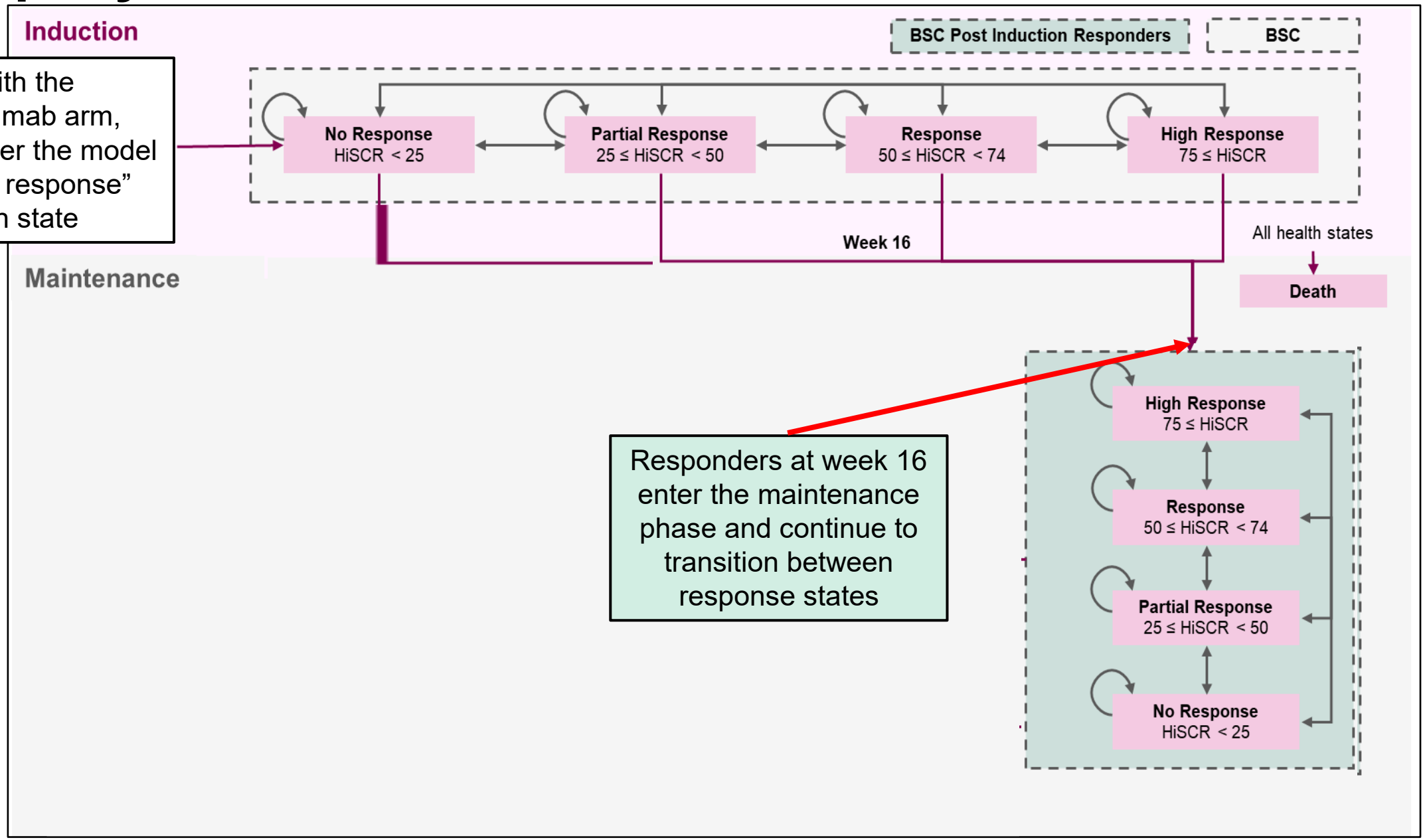
Company's Markov model – BSC arm

As with the secukinumab arm, patients enter the model in the "no response" health state



Responders at week 16 enter the maintenance phase and continue to transition between response states

Cost and QALY impact of secukinumab

- Technology affects **costs** by:
  - **Increased** treatment acquisition costs for secukinumab
  - **Decreased** health state costs for secukinumab
    - Improved treatment effectiveness → less time in more costly, lower HiSCR response health states

- Technology affects **QALYs** by:
  - **Increased** QALYs from more time spent in less severe health states
    - Improved treatment effectiveness → more time in higher HiSCR response health states
  - **Increased** QALYs from applying treatment specific health state utility values in the "no response" health state
    - In "no response state", people receiving secukinumab have higher QALYs than people receiving BSC. In other states, treatment pooled utility values are applied

- Assumptions with greatest **ICER** effect:
  - Source of BSC transition probabilities
  - Use of treatment specific vs treatment pooled health state utility values
  - Rates and unit costs of hospitalisations assumed for each model health state

Abbreviations: BSC, best supportive care; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year

Company's model inputs (1/2)

Input	Assumption and evidence source
Baseline characteristics	Based on SUNNY trials: • Mean age – 36.2 years; female (%) – 56.3%; mean weight – 93.47kg
Efficacy & extrapolation	**Induction phase (weeks 0 – 16):** • SUNNY trials, data from Q4W arm for secukinumab and placebo arm data for BSC **Up-titration phase (weeks 16-28, for non-responders in induction phase):** • SUNNY trials, Q2W arm for secukinumab • Not applicable for BSC **Maintenance phase (from end of induction/up-titration phase):** • SUNNY trials up to week 52 for secukinumab extrapolated over duration of model • PIONEER II (TA392) used for transition probabilities between week 16-52 and extrapolated over duration of model
Discontinuation	• All-cause discontinuation rates pooled from the SUNNY trials applied regardless of response during the maintenance phase • Per cycle discontinuation rate Year 1: [redacted], Year 2 onwards: 0.475%
Mortality	Based on age-matched general population mortality for all patients, irrespective of health state or treatment

Abbreviations: BSC, best supportive care; QxW, every x weeks.

Company's model inputs (2/2)

Input	Assumption and evidence source
Utilities	• EQ-5D-3L data collected between weeks 2-16 of the SUNNY trials • Utility values were assumed to be dependent on health state • In the non-response health state, utilities were also dependent on treatment • Utilities were age-adjusted using UK general population norms
Acquisition cost	• Costs of BSC include topical and oral antibiotics, dapsone, retinoids, ciclosporin and anti-androgens • Distribution of BSC treatments informed by clinical expert opinion
Administration cost	• One-off cost (£54.92) for training by a community-based nurse to self-administer
Health state costs and resource use	• Costs included for inpatient admissions, outpatient visits, wound care appointments and emergency care attendances • Resource use frequencies based on a survey of UK clinicians for TA392 • Resource use assumed to be health state specific and independent of treatment received
Severity	• Severity modifier not applied

Abbreviations: BSC, best supportive care; EQ-5D-3L, EuroQol 5 dimensions, 3 levels

Key issue: BSC transition probabilities (1/3)

Company and EAG disagree on data sources for BSC transition probabilities

Background

- Company's original model structure assumed that after week 16, people on BSC could only lose response, and could not regain a response for remainder of the model time horizon
- Company removed this assumption at technical engagement
- Company and EAG disagree on most appropriate source of data for BSC transition probabilities - has a large impact on ICER
- Comparison of company and EAG preferred sources for transition probabilities is presented in Table 1.

Table 1: Company and EAG preferred sources for transition probabilities

Model arm	Treatment phase	Company base case (post-TE)	EAG base case
SEC	Week 0-16	Week 0-16 data from secukinumab arm of SUNNY trials	
	Week 16-52 and Week 52+	Week 16-52 data from secukinumab arm of SUNNY trials	
BSC	Week 0-16	Week 0-16 data from placebo arm of SUNNY trials	
	Week 16-52 and Week 52+	**Week 12-36 data from placebo arm of PIONEER II study** (adalimumab vs BSC, used in TA392)	**Week 0-16 data from placebo arm of SUNNY trials**

Abbreviations: BSC, best supportive care; ICER, incremental cost-effectiveness ratio; SEC, secukinumab; TE, technical engagement.

Key issue: BSC transition probabilities (2/3)

Company prefers to use data from PIONEER II trials and EAG prefers data from SUNNY trials to estimate transition probabilities for BSC, after week 16

Company

- PIONEER II trial provides longer follow-up data than SUNNY trials for people treated with placebo (36 weeks versus 16 weeks)
- Approach is conservative as there are likely to be fewer non-responders to BSC in PIONEER II (TA392) as this population had not had prior biologics such as adalimumab
- Approach has been clinically validated – EAG's approach lacks face validity (see **Figure 1,** next slide)

EAG comments

- Company's approach relies on a naive comparison of placebo arms of SUNNY and PIONEER II studies and introduces bias as it breaks randomisation
- Although the concomitant treatments allowed in the placebo arms of the SUNNY and PIONEER were broadly similar, there are differences in baseline characteristics:
  - Population in PIONEER II had more severe disease at baseline but were less likely to have had previous surgery and no previous treatment with biologic therapies
  - Net effect of these differences is unclear
  - Follow-up duration in both studies is short
- The EAG present an alternative scenario assuming that people remain in the health state they were in at the last observed time point from the trial (52 weeks for secukinumab, 16 weeks for BSC)

Abbreviations: BSC, best supportive care.

Key issue: BSC transition probabilities (3/3)

Company's and EAG's assumptions for response over time

Figure 1: Proportion of responders over time with different model assumptions

Response definition:
Response is defined as the sum of health state occupancy proportions in the HiSCR50 to 74 and HiSCR≥75 states

Note: Although the same assumptions are used by the company and EAG for SEC, those who discontinue SEC go on to BSC. As the BSC assumptions in the company and EAG base cases are different, this means the SEC curves diverge over time because of discontinuations to BSC

Clinical experts: Which of the response curves look most plausible?
Committee: Should the transition probabilities for BSC be taken from week 12-36 data of PIONEER II (company base case), week 0-16 of the SUNNY trials (EAG base case), or be based on the last observation carried forward from the SUNNY trials (EAG scenario)?

Key issue: Alignment of costs and benefits for BSC (1/2)

Costs and benefits for BSC treatments are not aligned in company's model

Background

- Company used different sources for BSC costs and efficacy **(Table 1)**

Table 1: Company's BSC efficacy and cost assumptions and sources

BSC inputs in model	Description of BSC	Source
Efficacy	Simple pain management and restricted use of antibiotics	SUNNY and PIONEER II trials
Costs	Surgical procedures, topical and oral antibiotics, retinoids, dapsone, ciclosporin and anti-androgens	UK clinical opinion. Costs from prescription cost analysis (antibiotics) and eMIT

Company

- Updated its model structure at technical engagement to allow BSC patients to regain response once lost based on transition probabilities from PIONEER II (**previous key issue**)
- Model now addresses EAG's concerns as it captures the efficacy benefit of BSC treatments
- BSC treatments are supportive only, company's clinical experts support using data from placebo arm of SUNNY trials as a proxy for BSC efficacy in UK clinical practice

Abbreviations: BSC, best supportive care; eMIT, electronic market information tool.

Key issue: Alignment of costs and benefits for BSC (2/2)

EAG prefers to base BSC costs on treatments given in the placebo arms of SUNNY

EAG comments

- Although the revised model structure improves clinical validity and allows for the benefits of surgery and other BSC treatments to be included, these benefits are not quantified or explicitly modelled
- Costs of surgery and other BSC treatments used in UK practice are included in the model but the benefits are not
- The company assumes that PIONEER II data captures the benefit of these treatments, the EAG disagrees as the trial does not provide efficacy data for treatments given in UK practice
- Given that efficacy of treatments given in UK practice is unknown, the EAG base case uses costs based on treatments used in the placebo arm of the SUNNY trials (but still includes surgery costs)
- The EAG also provided a scenario where surgery costs are excluded to align completely with SUNNY trials

Clinical expert

- Small surgical procedures improve quality of life in the short term but do not alter natural disease history in terms of new skin lesions and progression of disease
- There is a lack of robust quality of life data for standard oral systemics (such as antibiotics)

Should the costs for the BSC arm of the model be aligned with the placebo arm of the SUNNY trials or with clinical expert opinion on UK clinical practice?

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Abbreviations: BSC, best supportive care

Key issue: Hospital resource use rates

Resource use estimates from survey of UK clinicians are uncertain

Background

- Hospital resource use rates for each model state based on survey of 40 UK clinical experts conducted for TA392
- Model predicts [redacted] and [redacted] surgeries over lifetime for BSC and secukinumab patients, respectively

Company

- Conducted clinical validation of TA392 estimates at technical engagement with 4 clinical experts:
  - 2 experts considered the resource use estimates appropriate, 1 considered them an underestimate and 1 provided no comment → Resource use likely to be an underestimate and conservative
- No published data available

EAG comments

- EAG and company base cases are the same, however EAG concerned that 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
- Conducted exploratory analyses reducing resource use estimates by 25%, 50%, 75% and 100% to explore the impact on the ICER

Clinical expert

- Resource use in HS may be underestimated due to miscoding, ~third of people with HS are undiagnosed

Has the uncertainty around hospital resource use rates been adequately captured?

Key issue: Health state utility values (1/2)

Background

- In original submission, company applied treatment-specific utilities in all health states
- → assumption that within the same health state, people on secukinumab had a higher utility than people on BSC
- EAG requested further data and analyses to support this assumption

Company

- Updated base case at technical engagement to include treatment specific utilities in the "no response" (HiSCR<25) health state **only**:
  - **Clinical data** – showed significant treatment effects of both Q2W and Q4W dose of secukinumab compared to placebo in the "no response" health state, in terms of:
    - percentage change in abscess and inflammatory nodule count from baseline
    - percentage of participants with no increase in abscesses at week 16
    - percentage of participants with no increase in draining fistula counts at week 16
  - **Statistical analyses** – a repeated measures regression model, with interaction terms for treatment and health state, showed a statistically significant treatment effect of the Q4W and Q2W secukinumab dose compared to placebo in the "no response" health state

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Abbreviations: BSC, best supportive care, HiSCR, hidradenitis suppurativa clinical response; QxW, every x weeks.

Key issue: Health state utility values (2/2)

EAG comments

- Satisfied with company's updated approach
- Noted that the Q2W dose also appears to have a significant effect on utility in the HiSCR25-49 and HiSCR50-74 states
- Company's and EAG's original utility values, and updated, agreed utility values after technical engagement are presented in **Table 1**

Table 1: Alternative health state utility values for application in the economic model

Treatment arm	Health state	Treatment specific (CS)	Treatment pooled (EAG report)	Treatment specific applied to "no response" health state only (company and EAG post-TE)
SEC Q4W	HiSCR≥75	[redacted]	[redacted]	[redacted]
	HiSCR50-74	[redacted]	[redacted]	[redacted]
	HiSCR25-49	[redacted]	[redacted]	[redacted]
	HiSCR<25	[redacted]	[redacted]	[redacted]
SEC Q2W	HiSCR≥75	[redacted]	[redacted]	[redacted]
	HiSCR50-74	[redacted]	[redacted]	[redacted]
	HiSCR25-49	[redacted]	[redacted]	[redacted]
	HiSCR<25	[redacted]	[redacted]	[redacted]
BSC	HiSCR≥75	[redacted]	[redacted]	[redacted]
	HiSCR50-74	[redacted]	[redacted]	[redacted]
	HiSCR25-49	[redacted]	[redacted]	[redacted]
	HiSCR<25	[redacted]	[redacted]	[redacted]

What are the most appropriate utility values: treatment specific, treatment pooled or treatment specific for the non-response health-state only?

Abbreviations: BSC, best supportive care; CS, company submission; HiSCR, hidradenitis suppurativa clinical response; QxW, every x weeks; SEC, secukinumab; TE, technical engagement.

Other issues: Inclusion of up-titration from Q4W to Q2W dose

EAG prefers not to model up-titration to Q2W dose

Company

- In model, people in secukinumab arm start on the Q4W dosing, non-responders at week 16 can up-titrate to Q2W dosing
- Efficacy for people who are up-titrated to Q2W regimen is based on the week 16-28 transition probabilities from all participants in the Q2W arms of the SUNNY trials
- Dosing in model is aligned with the anticipated marketing authorisation (maintenance dosing Q4W with the possibility to up-titrate to Q2W)
- If Q4W transition probabilities are used for non-responders who up-titrate to Q2W (rather than Q2W transition probabilities), the impact on the ICER is small

EAG comments

- Prefers not to model up-titration as the SUNNY trials were not designed to assess this, however the impact of including up-titration on the ICER is small (~£800/QALY decrease in EAG base case)
- Non-responders to the Q4W dose at week 16 are a more difficult to treat subgroup
- Therefore, applying effectiveness based on the full sample randomised to the Q2W dose likely over-estimates effectiveness in the subgroup who are more difficult to treat

Should up-titration be modelled? If so, what data / assumptions should be used?

NICE

Abbreviations: ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; QxW, every x weeks.

Other issues: Surgery costs

Company has aligned with EAG assumptions in TA392 to estimate cost of surgery, EAG prefers to assume most procedures will be minor

Company

- Approach to costing surgery aligned with that used by EAG in TA392
- Presented additional scenarios assuming different numbers of lifetime wide excisions (elective inpatient, major surgeries) and exploring the impact of reducing the proportion of day-case surgeries

EAG comments

- Company's updated approach (and scenarios) excludes minor procedures
- Most procedures for HS are minor, therefore the company's approach may still overestimate costs
- EAG prefers to derive the surgery cost by weighting across all grades of procedure and across day-case and elective inpatient settings
- A comparison of approaches and final costs applied in the model is presented in **Table 1**

Table 1: Company and EAG approach to costing surgery

Setting	Type of skin procedure	Company post-TE	EAG
Elective inpatient	Multiple major	0%	0.13%
	Major	6.68%	0.52%
	Intermediate	13.16%	1.85%
	Minor	0%	0.87%
Day case	Multiple major	0%	1.02%
	Major	0%	3.68%
	Intermediate	67.00%	22.25%
	Minor	0%	69.68%
Non-elective short stay	Intermediate	13.16%	0%
Weighted average cost		**£2,401.52**	**£1,216.68**

Are the company or EAG estimates for the cost of surgery more appropriate?

Other issues: Outpatient visit frequencies

The company's estimates of resource use may double count outpatient visits

Background

- The EAG was concerned that company's estimates of hospital resource use may double count resource use for outpatient appointments as "outpatient visits for HS surgery" or "visits to wound care" may already be included in "outpatient visits for any reason"

Company

- Approach to estimating resource use is aligned with TA392 where all of these components were included as separate resource use categories

EAG comments

- The EAG retains its preference to only include one set of outpatient costs
- Impact on ICER is small
- There are remaining uncertainties with the company's estimates of resource use in general (see key issue)

Are the company or EAG estimates for resource use more appropriate?

Abbreviations: ICER, incremental cost-effectiveness ratio.

Summary of company and EAG base case assumptions

Assumption	Company base case	EAG base case
BSC transition probabilities	Based on placebo arms of SUNNY and TA392 Responders* at 1, 5 and 10 years in BSC arm; [redacted], [redacted] and [redacted], respectively.	Based on placebo arms of SUNNY Responders* at 1, 5 and 10 years in BSC arm; [redacted].
Health-state utility values	Treatment specific for "no response" state only	
Hospital resource use rates	Survey of n=40 UK clinical experts conducted for TA392	
BSC costs	UK clinical opinion	Placebo arms of SUNNY trials
Up-titration to Q2W dose permitted	Yes	No
Surgery cost	As per TA392 – no minor procedures (£2,402)	Weighted across HRG codes for all grades of surgery (£1,217)
Outpatient visit frequencies	TA392	TA392 – with some outpatient visits removed to avoid double counting
Prescribing setting for BSC treatments	Most antibiotics prescribed in primary care, all other treatments prescribed in secondary care	

Notes: *Response is defined as the sum of health state occupancy proportions in the HiSCR50-74 and HiSCR≥75 states. **Abbreviations:** BSC, best supportive care; HRG, healthcare resource group; Q2W, every 2 weeks.

Company base case results

Company deterministic base case results

Technology	Total costs (£)	Total QALYs	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)
BSC	[redacted]	[redacted]			
Secukinumab	[redacted]	[redacted]	[redacted]	[redacted]	£42,415

Company probabilistic base case results

Technology	Total costs (£)	Total QALYs	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)
BSC	[redacted]	[redacted]			
Secukinumab	[redacted]	[redacted]	[redacted]	[redacted]	£42,268

Abbreviations: BSC, best supportive care; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

EAG base case results

EAG deterministic base case results

Technology	Total costs (£)	Total QALYs	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)
BSC	[redacted]	[redacted]			
Secukinumab	[redacted]	[redacted]	[redacted]	[redacted]	£95,821

EAG probabilistic base case results

Technology	Total costs (£)	Total QALYs	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)
BSC	[redacted]	[redacted]			
Secukinumab	[redacted]	[redacted]	[redacted]	[redacted]	£96,353

Abbreviations: BSC, best supportive care; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

Company and EAG base case results

Individual impact of EAG preferences on company ICER (deterministic)

No.	EAG preference (applied individually to company base case)	Incremental costs (£) versus BSC	Incremental QALYs versus BSC	ICER (£/QALY) versus BSC
0	**Company base case**	[redacted]	[redacted]	£42,415
1	BSC transition probabilities beyond week 16 extrapolated from SUNNY trials	[redacted]	[redacted]	£86,504
2	EAG's preferred surgery costing approach	[redacted]	[redacted]	£45,847
3	BSC costs as per placebo arms of SUNNY trials	[redacted]	[redacted]	£45,091
4	Up-titration removed	[redacted]	[redacted]	£43,412
5	EAG's preferred outpatient visit frequencies	[redacted]	[redacted]	£43,294
6	EAG preferred base case (combined 0-6)	[redacted]	[redacted]	£95,821

Abbreviations: BSC, best supportive care; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

Company deterministic scenario analysis

Company scenario analyses (deterministic)

No.	Scenario (applied to company base case)	Incremental costs (£) versus BSC	Incremental QALYs versus BSC	ICER (£/QALY) versus BSC
1	**Company base case**	[redacted]	[redacted]	£42,415
2	2 lifetime wide excisions, 49% surgeries as intermediate as day case with the reminder intermediate inpatient days	[redacted]	[redacted]	£42,022
3	3 lifetime wide excisions, 49% surgeries as intermediate as day case with the reminder intermediate inpatient days	[redacted]	[redacted]	£41,285
4	4 lifetime wide excisions, 49% surgeries as intermediate as day case with the reminder intermediate inpatient days	[redacted]	[redacted]	£40,548

NICE

Abbreviations: BSC, best supportive care; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

EAG deterministic scenario analysis (1/2)

EAG scenario analyses (deterministic)

No.	Scenario (applied to EAG base case)	Incremental costs (£) versus BSC	Incremental QALYs versus BSC	ICER (£/QALY) versus BSC
1	**EAG base case**	[redacted]	[redacted]	£95,821
2	Assume 2 lifetime wide excisions, 49% surgeries as intermediate day case, with remainder as intermediate inpatient.	[redacted]	[redacted]	£92,303
3	Assume 3 lifetime wide excisions, 49% surgeries as intermediate day case, with remainder as intermediate inpatient.	[redacted]	[redacted]	£91,625
4	Assume 4 lifetime wide excisions, 49% surgeries as intermediate day case, with remainder as intermediate inpatient.	[redacted]	[redacted]	£90,947

Abbreviations: BSC, best supportive care; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

EAG deterministic scenario analysis (2/2)

EAG scenario analyses (deterministic)

No.	Scenario (applied to EAG base case)	Incremental costs (£) versus BSC	Incremental QALYs versus BSC	ICER (£/QALY) versus BSC
1	**EAG base case**	[redacted]	[redacted]	£95,821
5	Reduce non-surgery resource use by 25%	[redacted]	[redacted]	£97,100
6	Reduce non-surgery resource use by 50%	[redacted]	[redacted]	£98,379
7	Reduce non-surgery resource use by 75%	[redacted]	[redacted]	£99,658
8	Reduce non-surgery resource use by 100%	[redacted]	[redacted]	£100,937
9	Reduce surgery resource use by 25%	[redacted]	[redacted]	£96,631
10	Reduce surgery resource use by 50%	[redacted]	[redacted]	£97,442
11	Reduce surgery resource use by 75%	[redacted]	[redacted]	£98,252
12	Reduce surgery resource use by 100%	[redacted]	[redacted]	£99,062
13	Long-term extrapolations based on last observation carried forward from the both arms of SUNNY trials	[redacted]	[redacted]	£68,135

Abbreviations: BSC, best supportive care; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.