NICE National Institute for Health and Care Excellence

Single Technology Appraisal

Secukinumab for treating non-radiographic axial spondyloarthritis [ID1419]

Committee Papers

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

SINGLE TECHNOLOGY APPRAISAL

Secukinumab for treating non-radiographic axial spondyloarthritis [ID1419]

Contents:

The following documents are made available to consultees and commentators:

Any information supplied to NICE which has been marked as confidential, has been redacted. All personal information has also been redacted.

Secukinumab for treating non-radiographic axial spondyloarthritis

Single Technology Appraisal

Response to consultee, commentator and public comments on the Appraisal Consultation Document (ACD)

Type of stakeholder:

Consultees – Organisations that accept an invitation to participate in the appraisal including the companies, national professional organisations, national patient organisations, the Department of Health and Social Care and the Welsh Government and relevant NHS organisations in England. Consultees can make a submission and participate in the consultation on the appraisal consultation document (ACD; if produced). All non-company consultees can nominate clinical experts and/or patient experts to verbally present their personal views to the Appraisal Committee. Company consultees can also nominate clinical experts. Representatives from NHS England and clinical commissioning groups invited to participate in the appraisal may also attend the Appraisal Committee as NHS commissioning experts. All consultees have the opportunity to consider an appeal against the final recommendations, or report any factual errors, within the final appraisal document (FAD).

Clinical and patient experts and NHS commissioning experts – The Chair of the Appraisal Committee and the NICE project team select clinical experts and patient experts from nominations by consultees and commentators. They attend the Appraisal Committee meeting as individuals to answer questions to help clarify issues about the submitted evidence and to provide their views and experiences of the technology and/or condition. Before they attend the meeting, all experts must either submit a written statement (using a template) or indicate they agree with the submission made by their nominating organisation..

Commentators – Commentators can participate in the consultation on the ACD (if produced), but NICE does not ask them to make any submission for the appraisal. Non-company commentator organisations can nominate clinical experts and patient experts to verbally present their personal views to the Appraisal Committee. Commentator organisations representing relevant comparator technology companies can also nominate clinical experts. These organisations receive the FAD and have opportunity to report any factual errors. These organisations include comparator technology companies, Healthcare Improvement Scotland any relevant National Collaborating Centre (a group commissioned by NICE to develop clinical guidelines), other related research groups where appropriate (for example, the Medical Research Council and National Cancer Research Institute); other groups such as the NHS Confederation, the NHS Commercial Medicines Unit, the Scottish Medicines Consortium, the Medicines and Healthcare Products Regulatory Agency, the Department of Health and Social Care, Social Services and Public Safety for Northern Ireland).

Public – Members of the public have the opportunity to comment on the ACD when it is posted on the Institute's web site 5 days after it is sent to consultees and commentators. These comments are usually presented to the appraisal committee in full, but NICE reserves the right to summarise and edit comments received during consultations, or not to publish them at all, where in the reasonable opinion of NICE, the comments are voluminous, publication would be unlawful or publication would be otherwise inappropriate.

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment number	Type of stakeholder	Organisation name	Stakeholder comment Please insert each new comment in a new row	NICE Response Please respond to each comment
1.	Comparator company	UCB pharma	**Section 3.3 Positioning of secukinumab:** UCB agrees with the opinion of the clinical expert presented at the committee meeting. It is not ideal to cycle people with axSpA through TNF inhibitors when they have achieved inadequate response to a previous TNF inhibitor. The ERG on this appraisal favoured using assumptions on future TNF efficacy in line with TA383. These analyses use data from people with rad-axSpA in the DANBIO registry (Glintborg et al. 2013). This registry shows a marked decrease in the efficacy of TNF inhibitors given in sequence. Glintborg et al. 2013 analysed patients who had both 3 and 6 month BASDAI50 data, which excludes patients who have primary non-response (a more favourable subgroup than all patients with inadequate response), and found that median time to drug discontinuation on second line TNF inhibitors was reduced from 3.1 to 1.6 years and that, in patients who switched TNF inhibitors, first line BASDAI50 response was 54% while second line response was only 37% and third line response was 30%. In people with axSpA whose axSpA does not respond to TNF inhibitor treatment within the first 3 to 6 months, response rates on second line TNF inhibitors would be expected to be lower. These DANBIO data support the clinical expert's position that patients who respond inadequately to first-line TNF inhibitors should be tried on treatments with a different mechanism of action such as IL-17s rather than additional TNF inhibitors.	Thank you for your comments supporting the clinical expert's position described in the Appraisal Consultation Document (ACD). No changes required.
2.	Comparator company	UCB pharma	**Section 3.10: Cost of TNF-inhibitors as a drug class:** Given the low price of adalimumab biosimilar, UCB agrees with clinical opinion stating that adalimumab biosimilar is likely to be the first line biologic of choice. Given heterogeneity in the patient	Thank you for your comments. The committee noted and accepted that adalimumab biosimilar may not be appropriate for first line use for some

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			population, setting price assuming that 100% of patients would take biosimilar adalimumab at 1st line is inappropriate. A more appropriate assumption should be based on the goals and performance of the NHSE framework pricing agreement on biosimilar adalimumab. From October 2018 to May 2019, the share of biosimilar adalimumab as first or second biologic across a wide number of indications increased to 63%. The goal of the NHSE framework was to increase this to 80%. A value of 80% should be considered a natural cap on adalimumab market share at first line. This necessarily means that biosimilar adalimumab will not be the treatment of choice for most new second line patients. UCB rejects the assumption that 1st line treatment costs should represent a 100% market share for biosimilar adalimumab, as this biases the analysis substantially in favour of TNF inhibitors. At a minimum, this assumption should be tested in sensitivity analyses. In TA383, NICE analysed TNF inhibitors as being of equivalent efficacy, but also acknowledged that some treatments are better for different patient profiles and that choice of 1st line biologic should be driven by the appropriateness of the therapy to the patient. Adalimumab will not be the most suitable treatment for all patients.	patients in clinical practice (Final Appraisal Document (FAD) 3.3, 3.10) We have amended the wording in section 3.10 to note that the uptake of the adalimumab biosimilar may not be 100% in clinical practice across all of its indications.
3.	Comparator company	UCB pharma	**Section 3.10 Etanercept as preferred 2nd line TNF:** As in the above point, costing all TNF inhibitors using only one member of the class biases the analysis in favour of TNF inhibitors. Given prescribers should first consider which treatment is most appropriate for patients, cost of the lowest cost biosimilar should not be the only driver of market share calculations. Moreover, etanercept, as noted by the clinical expert, is contraindicated in patients with uveitis, and some patients are contraindicated for TNF inhibitors, in general. It is also the case that patients should be given some voice in their choice of treatment, and many patients are more comfortable with less frequent injections. Etanercept has more frequent injections than other TNF inhibitors.	Thank you for your comments. The committee considered it appropriate to consider TNF-alpha inhibitors as a class because they have broadly similar clinical effectiveness (see section 3.8 of FAD). It noted however (see section 3.10 of the FAD) that the TNF-alpha inhibitors have very different costs and the NICE recommendations for TNF-alpha inhibitors state that when more than 1 TNF-alpha inhibitors are suitable, the least expensive should be

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			Market data at 2nd line is likely to be more appropriate than assuming 100% etanercept costs.	chosen. If etanercept is contra-indicated the next available cheapest TNF-alpha inhibitor should be offered to patients.
5.	Company	Novartis Pharmaceuticals UK Ltd	**Draft recommendation:** We agree with the draft recommendation and welcome the committee's decision to recommend secukinumab as a first line biologic option in certain circumstances, and as a second line option for patients with inadequate response to tumour necrosis factor-alpha inhibitors. This recommendation for secukinumab will give clinicians and patients freedom to choose the most appropriate treatment given each individual patient's particular circumstances.	Thank you for your comments. No changes required.
6.	Company	Novartis Pharmaceuticals UK Ltd	**Clinical trial results** Novartis comment: Although not all trial statistics are published, most secondary outcome results are published and were not marked confidential in the company submission. Requested amendments: Page 8 Current wording: • "Secukinumab increased the proportion of people who had an ASAS 40 response compared with placebo (odds ratio [OR] 1.72, p<0.0197; 95% confidence intervals and secondary outcome results are confidential and cannot be reported here)" Proposed wording:	Thank you for your comments. The editorial change suggested by the company has been applied in the FAD (3.4).

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			• "Secukinumab increased the proportion of people who had an ASAS 40 response compared with placebo (odds ratio [OR] 1.72, p<0.0197; 95% confidence intervals are confidential and cannot be reported here)"	
7.	Company	Novartis Pharmaceuticals UK Ltd	**Results of the indirect comparison** **Novartis comment:** There were limitations to the indirect comparisons, including several sources of heterogeneity across the trials that might explain the smaller effect estimates for secukinumab (including baseline C-reactive protein levels and the proportion of patients who had previously received a tumour necrosis factor-alpha inhibitor). PREVENT also had a higher overall mean baseline Bath Ankylosing Spondylitis Functional Index value; this is expected to lead to conservative estimates of secukinumab efficacy, as acknowledged in Paragraph 3.6 of the Appraisal Consultation Document. Placebo response rates were also higher in PREVENT than in older trials of tumour necrosis factor-alpha inhibitors. The network meta-analysis findings represent the most robust estimate of relative treatment efficacy of secukinumab versus other biologics. However, given the limited evidence available, it is not possible to quantify the influence/impact of the identified factors (i.e. potential treatment-effect modifiers) upon the network meta-analysis results. Novartis agrees with the committee's interpretation of the network meta-analysis results outlined in paragraph 3.8 i.e. that credible intervals were wide and "there were no statistically significant differences". In clinical practice, secukinumab efficacy is not expected to differ substantially from tumour necrosis factor-alpha inhibitors, as supported by the clinical expert and documented in Paragraph 3.8. **Requested amendments:**	Thank you for your comments. Please see response to suggested wording changes below.

Comment number	Type of stakeholder	Organisation name	Stakeholder comment Please insert each new comment in a new row	NICE Response Please respond to each comment
			Page 4 Current wording: • "But an indirect comparison suggests that secukinumab may be less effective than TNF-alpha inhibitors." Proposed wording: • "Based on indirect comparisons, point estimates for clinical effectiveness favoured TNF-alpha inhibitors over secukinumab on some outcomes, although with wide overlapping credible intervals and no statistically significant differences."	This summary is a short overview in plain English and does not require any changes. The following sentence in the summary is "However, this evidence is uncertain" which highlights the uncertainty in the results. A detailed description of the uncertainties and lack of statistical significance are described in section 3.8 of the FAD. It is also noted that the company's model shows fewer QALYs for secukinumab than TNF-alpha inhibitors.
8.	Company	Novartis Pharmaceuticals UK Ltd	**Results of the cost-effectiveness analysis** **Novartis comment:** The conclusion that secukinumab is not cost-effective versus tumour necrosis factor-alpha inhibitors is based on the Evidence Review Group analyses, in which a single efficacy estimate is used for all tumour necrosis factor-alpha inhibitors and the cost of biosimilar adalimumab is assumed for all tumour necrosis factor-alpha inhibitors. The Novartis base case allowed for differing efficacy between tumour necrosis factor-alpha inhibitors and considered the costs of each treatment separately. The Novartis base case results (Table 82 of the Company Submission) showed secukinumab to be highly cost-effective versus golimumab (including free stock as part of the complex	**Thank you for your comments.** Please see response to suggested wording changes below.

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			patient access scheme), certolizumab pegol (including free stock as part of the complex patient access scheme), and etanercept (at list price). Since confidential simple patient access schemes are not in place for golimumab and certolizumab pegol, Novartis is confident that secukinumab is both of similar efficacy and less expensive than these two tumour necrosis factor-alpha inhibitors, both of which are recommended by the National Institute for Health and Care Excellence as first line biologic options (1, 2). However, Novartis recognises that biosimilar adalimumab is now the most widely used tumour necrosis factor-alpha inhibitor in clinical practice in the United Kingdom. We therefore accept the committee's draft recommendations, but request that all relevant wording is amended to make clear that statements on the cost-effectiveness of secukinumab are based on assuming the costs of biosimilar adalimumab for all tumour necrosis factor-alpha inhibitors. **Requested amendments:** <u>Page 4</u> Current wording: • "Secukinumab is only considered to be a cost-effective use of NHS resources for people who cannot have TNF-alpha inhibitors, or when TNF-alpha inhibitors have not worked well enough." Proposed wording: • "When costs of TNF-alpha inhibitors are informed by those of biosimilar adalimumab, secukinumab is only considered to be a cost-effective use of NHS resources for people who cannot have TNF-alpha inhibitors, or when TNF-alpha	A variation of the editorial change suggested by the company has been made to the "why the committee made these recommendations" in the FAD. Different TNF-alpha inhibitors have different costs but similar clinical effectiveness. When more than one TNF-alpha inhibitor is suitable, the cheapest is used, currently adalimumab biosimilar. Because of this, secukinumab is not a cost-effective use of NHS resources when compared with

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			inhibitors have not worked well enough. Secukinumab would be considered cost-effective versus branded TNF-alpha inhibitors (such as golimumab and certolizumab pegol), although these are understood not to be widely used as first line biologics in UK clinical practice” <u>Page 15</u> Current heading wording: • “Secukinumab is more costly and less effective than TNF-alpha inhibitors.” Proposed heading wording: • “Secukinumab is more costly and less effective than biosimilar TNF-alpha inhibitors” Proposed clarification in subsequent text: • “In analyses that assume a single efficacy estimate and the costs of biosimilar adalimumab for all TNF-alpha inhibitors, secukinumab is more costly and less effective than TNF-alpha inhibitors. Secukinumab is less costly and is more cost-effective versus certain branded TNF-alpha inhibitors i.e. golimumab and certolizumab pegol”. <u>Page 15</u> Current wording:	TNF-alpha inhibitors. The editorial change suggested by the company has been reflected in the text in section 3.14 of the FAD. The committee concluded that secukinumab had fewer QALYs in all the company and ERG’s analyses. The committee noted that in analyses where the cost of biosimilar adalimumab is assumed for all TNF-alpha inhibitors, the costs of secukinumab were also higher than TNF-alpha inhibitors.

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			• "The committee did not consider the difference in QALYs to be minimal and noted in most analyses the costs of secukinumab were also higher than TNF-alpha inhibitors." Proposed wording: • "The committee did not consider the difference in QALYs to be minimal and noted that in analyses where the cost of biosimilar adalimumab is assumed for all TNF-alpha inhibitors, the costs of secukinumab were also higher than TNF-alpha inhibitors." <u>Page 16</u> Current wording: • "The costs for secukinumab are generally higher than for TNF-alpha inhibitors." Proposed wording: "The costs for secukinumab are higher than for biosimilar TNF-alpha inhibitors, such as adalimumab and etanercept, but lower than branded TNF-alpha inhibitors i.e. golimumab and certolizumab pegol	Section 3.16 of the FAD has been updated to: … secukinumab gave fewer QALYs than biosimilar TNF-alpha inhibitors. [the committee] also noted that the costs for secukinumab were higher than biosimilar TNF-alpha inhibitors, which are used first line when 1 or more inhibitors are suitable, because of their lower cost.
9.	Company	Novartis Pharmaceuticals UK Ltd	**Second-line analyses** **Novartis comment:** The Novartis model presented results in patients with and without prior exposure to tumour necrosis factor-alpha inhibitors (tumour	Thank you for your comments. Please see response to suggested wording amendment below.

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			necrosis factor-experienced, or 2nd line, and tumour necrosis factor-naïve, or 1st line) based on the subgroups in PREVENT. A primary cost-effectiveness analysis was presented for tumour necrosis factor-naïve patients (informed by the network meta-analysis), and a secondary cost-effectiveness analysis was presented for tumour necrosis factor-experienced patients (informed by PREVENT data) (Section 3.8 of the Company Submission). Inclusion criteria for the PREVENT trial included the following: • Patients who had been on a tumour necrosis factor-alpha inhibitor (not more than one) had to have experienced an inadequate response to previous or current treatment given at an approved dose for at least 3 months prior to randomisation, or had been intolerant to at least one administration of an anti-tumour necrosis factor-alpha agent. The cost-effectiveness analysis for the second-line population therefore included both individuals who had responded inadequately to tumour necrosis factor-alpha inhibitors and those who were intolerant to at least one dose of a tumour necrosis factor-alpha inhibitor. **Requested amendments:** <u>Page 12:</u> Current wording: • "The company model only included the population in PREVENT who had not had TNF-alpha inhibitors before. The model therefore related only to first-line use of secukinumab. No base-case analysis for the subgroup who	Sction 3.9 has been updated to state: However, [the ERG] noted that the primary analysis modelled by the company only included the population in PREVENT who had not had TNF-alpha inhibitors before, so related only to first-line use of secukinumab. The company also presented a secondary

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			cannot have TNF-alpha inhibitors or whose disease responded inadequately to these was presented by the company." Proposed wording: • "The company model included a primary analysis considering the population in PREVENT who had not had TNF-alpha inhibitor before, and a secondary analysis considering the population in PREVENT who had received one prior TNF-alpha inhibitor". <u>Page 16</u> Current wording: • "[The committee] noted that it had only been presented with cost-effectiveness estimates for secukinumab compared with conventional care for the whole population but considered that secukinumab was likely to be a cost-effective use of NHS resources for people who cannot have TNF-alpha inhibitors. There were no data to determine if these results would be different in the subgroup of people who cannot have TNF-alpha inhibitors or whose condition had not responded to a TNF-alpha inhibitor." Proposed wording: "[The committee] noted that it had only been presented with cost-effectiveness estimates for secukinumab compared with	analysis, which included the small subgroup of people in PREVENT who had treatment with 1 TNF-alpha inhibitor before. No base-case analysis for the subgroup who cannot have TNF-alpha inhibitors was presented by the company. A variation of the editorial change suggested by the company has been applied to the text in the FAD (3.15) That is: the committee noted that these estimates were for the whole population, not just people for whom TNF-alpha inhibitors were contraindicated or unsuitable. There

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			conventional care for the full second line (biologic-experienced) population; no subgroup analysis was presented in people who are contraindicated for, or who cannot have, TNF-alpha inhibitors. The Committee considered that secukinumab was likely to be a cost-effective use of NHS resources for people who cannot have TNF-alpha inhibitors. There were no data to determine if these results would be different in the subgroup of people who cannot have TNF-alpha inhibitors versus the subgroup whose condition had not responded to a TNF-alpha inhibitor."	were no data to determine if these results would be different in the subgroup of people who cannot have TNF-alpha inhibitors or whose condition had not responded to a TNF-alpha inhibitor. However, given the ICERs were lower than £20,000 compared with conventional care in the whole population, it was reasonable to consider secukinumab a cost-effective use of NHS resources for people who would otherwise have conventional care.
10.	Company	Novartis Pharmaceuticals UK Ltd	**Company model** **Novartis comment:** In the company submission, the Novartis model considered each individual tumour necrosis factor-alpha inhibitor as a separate treatment option. Following a clarification question from the Evidence Review Group, an additional scenario was provided where a single tumour necrosis factor-alpha inhibitor comparator was included, and a weighted average drug cost was generated based on confidential market share information. **Requested amendments:** <u>Page 12</u> Current wording: • "The company used an average of confidential market	Thank you for your comments. Please see response to suggested wording amendment below. Section 3.8 of the FAD notes that the company presented results comparing secukinumab with each individual TNF-

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			share information to cost TNF-alpha inhibitors. It used a single comparator to reflect the effect of TNF-alpha inhibitors as a drug class, and when considering the effect of subsequent treatment with a TNF-alpha inhibitor in the economic model". Proposed wording: "In the company base-case, each TNF-alpha inhibitor was considered as a separate treatment option. Following a request from the ERG, a scenario was provided in which the company used an average of confidential market share information to cost TNF-alpha inhibitors and a single comparator was used to reflect the effect of TNF-alpha inhibitors as a drug class, and when considering the effect of subsequent treatment with a TNF-alpha inhibitor in the economic model".	alpha inhibitor, and with TNF-alpha inhibitors as a drug class. The rationale for committee's preference for the comparison with TNF-alpha inhibitors as a drug class is given in section 3.8
11.	Company	Novartis Pharmaceuticals UK Ltd	**Patients for whom secukinumab may be the most suitable first-line choice** **Novartis comment:** We agree with the statements on Page 7 that "for disease that has had an inadequate response to TNF-alpha inhibitors, it is preferable to try a new treatment option with an alternative mechanism of action" and that "secukinumab is more effective than TNF-alpha inhibitors for treating psoriasis." We also understand from clinical experts that there are several reasons why first-line treatment with secukinumab may be the right choice for a patient, including: • its suitability for patients with multiple sclerosis or tuberculosis • its safety profile – in randomised controlled trials and in the	Thank you for your comments agreeing with the statements in the ACD. No changes required.

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			real-world setting secukinumab has consistently demonstrated a safety profile with very low infection and cancer risk (3) • its administration frequency – monthly administration of secukinumab may be preferential for some patients.	
12.	Company	Novartis Pharmaceuticals UK Ltd	**Biosimilar terminology** **Requested amendments:** <u>Page 7</u> Current wording: • "given the extensive clinical experience with TNF-alpha inhibitors and the lower price of generic versions now available". Proposed wording: "given the extensive clinical experience with TNF-alpha inhibitors and the lower price of biosimilar versions now available".	The editorial change suggested by the company has been applied to the text in the FAD (3.3).
14.	Web comment	NICE medicines team	This comment doesn't relate specifically to this TA but is something I picked up on when reviewing it. On checking NG65 on Spondyloarthritis in over 16s (to see where the info on which TNF-alpha inhibitors are recommended for axial spondyloarthritis came from), I could not see any recommendations relating to using golimumab for non-radiographic axial spondyloarthritis. The only rec in that guideline(1.4.3) appears to relate to treating severe active ankylosing spondylitis. However, on searching the NICE website I can see there is a TA for golimumab for non-radiographic axial spondyloarthritis (TA 497). Does TA 497 need incorporating into NG65? Assume this TA when published will also be incorporated into NG65?	Thank you for your comment. TA 497 was issued after the last review of NG65. NICE guidelines are routinely reviewed and the incorporation of TA497 and the current appraisal guidance into NG65 will be considered when NG65 is reviewed.

NICE National Institute for Health and Care Excellence

Secukinumab for treating non-radiographic axial spondyloarthritis [ID1419]

Consultation on the appraisal consultation document – deadline for comments 5pm on Tuesday 20 April 2021 **email:** NICE DOCS

	Please read the checklist for submitting comments at the end of this form. We cannot accept forms that are not filled in correctly. The Appraisal Committee is interested in receiving comments on the following: • has all of the relevant evidence been taken into account? • are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence? • are the provisional recommendations sound and a suitable basis for guidance to the NHS? NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the preliminary recommendations may need changing in order to meet these aims. In particular, please tell us if the preliminary recommendations: • could have a different impact on people protected by the equality legislation than on the wider population, for example by making it more difficult in practice for a specific group to access the technology; • could have any adverse impact on people with a particular disability or disabilities. Please provide any relevant information or data you have regarding such impacts and how they could be avoided or reduced**.**
Organisation name – Stakeholder or respondent (if you are responding as an individual rather than a registered stakeholder please leave blank):	Novartis Pharmaceuticals UK Limited
Disclosure Please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry.	None
Name of commentator person completing form:	[redacted]

Please return to: **NICE DOCS**

NICE National Institute for Health and Care Excellence

Secukinumab for treating non-radiographic axial spondyloarthritis [ID1419]

Consultation on the appraisal consultation document – deadline for comments 5pm on Tuesday 20 April 2021 **email:** NICE DOCS

Comment number	Comments Insert each comment in a new row. Do not paste other tables into this table, because your comments could get lost – type directly into this table.
1	**Draft recommendation** **Novartis comment:** We agree with the draft recommendation and welcome the committee's decision to recommend secukinumab as a first line biologic option in certain circumstances, and as a second line option for patients with inadequate response to tumour necrosis factor-alpha inhibitors. This recommendation for secukinumab will give clinicians and patients freedom to choose the most appropriate treatment given each individual patient's particular circumstances.
2	**Clinical trial results** **Novartis comment:** Although not all trial statistics are published, most secondary outcome results are published and were not marked confidential in the company submission. **Requested amendments:** <u>Page 8</u> Current wording: • "Secukinumab increased the proportion of people who had an ASAS 40 response compared with placebo (odds ratio [OR] 1.72, p<0.0197; 95% confidence intervals and secondary outcome results are confidential and cannot be reported here)" Proposed wording: • "Secukinumab increased the proportion of people who had an ASAS 40 response compared with placebo (odds ratio [OR] 1.72, p<0.0197; 95% confidence intervals are confidential and cannot be reported here)"
3	**Results of the indirect comparison** **Novartis comment:** There were limitations to the indirect comparisons, including several sources of heterogeneity across the trials that might explain the smaller effect estimates for secukinumab (including baseline C-reactive protein levels and the proportion of

	patients who had previously received a tumour necrosis factor-alpha inhibitor). PREVENT also had a higher overall mean baseline Bath Ankylosing Spondylitis Functional Index value; this is expected to lead to conservative estimates of secukinumab efficacy, as acknowledged in Paragraph 3.6 of the Appraisal Consultation Document. Placebo response rates were also higher in PREVENT than in older trials of tumour necrosis factor-alpha inhibitors. The network meta-analysis findings represent the most robust estimate of relative treatment efficacy of secukinumab versus other biologics. However, given the limited evidence available, it is not possible to quantify the influence/impact of the identified factors (i.e. potential treatment-effect modifiers) upon the network meta-analysis results. Novartis agrees with the committee's interpretation of the network meta-analysis results outlined in paragraph 3.8 i.e. that credible intervals were wide and "there were no statistically significant differences". In clinical practice, secukinumab efficacy is not expected to differ substantially from tumour necrosis factor-alpha inhibitors, as supported by the clinical expert and documented in Paragraph 3.8. **Requested amendments:** <u>Page 4</u> Current wording: • "But an indirect comparison suggests that secukinumab may be less effective than TNF-alpha inhibitors." Proposed wording: • "Based on indirect comparisons, point estimates for clinical effectiveness favoured TNF-alpha inhibitors over secukinumab on some outcomes, although with wide overlapping credible intervals and no statistically significant differences."
4	**Results of the cost-effectiveness analysis** **Novartis comment:** The conclusion that secukinumab is not cost-effective versus tumour necrosis factor-alpha inhibitors is based on the Evidence Review Group analyses, in which a single efficacy estimate is used for all tumour necrosis factor-alpha inhibitors and the cost of biosimilar adalimumab is assumed for all tumour necrosis factor-alpha inhibitors. The Novartis base case allowed for differing

	efficacy between tumour necrosis factor-alpha inhibitors and considered the costs of each treatment separately. The Novartis base case results (Table 82 of the Company Submission) showed secukinumab to be highly cost-effective versus golimumab (including free stock as part of the complex patient access scheme), certolizumab pegol (including free stock as part of the complex patient access scheme), and etanercept (at list price). Since confidential simple patient access schemes are not in place for golimumab and certolizumab pegol, Novartis is confident that secukinumab is both of similar efficacy and less expensive than these two tumour necrosis factor-alpha inhibitors, both of which are recommended by the National Institute for Health and Care Excellence as first line biologic options (1, 2). However, Novartis recognises that biosimilar adalimumab is now the most widely used tumour necrosis factor-alpha inhibitor in clinical practice in the United Kingdom. We therefore accept the committee's draft recommendations, but request that all relevant wording is amended to make clear that statements on the cost-effectiveness of secukinumab are based on assuming the costs of biosimilar adalimumab for all tumour necrosis factor-alpha inhibitors. **Requested amendments:** <u>Page 4</u> Current wording: • "Secukinumab is only considered to be a cost-effective use of NHS resources for people who cannot have TNF-alpha inhibitors, or when TNF-alpha inhibitors have not worked well enough." Proposed wording: • "When costs of TNF-alpha inhibitors are informed by those of biosimilar adalimumab, secukinumab is only considered to be a cost-effective use of NHS resources for people who cannot have TNF-alpha inhibitors, or when TNF-alpha inhibitors have not worked well enough. Secukinumab would be considered cost-effective versus branded TNF-alpha inhibitors (such as golimumab and certolizumab pegol), although these are understood not to be widely used as first line biologics in UK clinical practice" <u>Page 15</u> Current heading wording: • "Secukinumab is more costly and less effective than TNF-alpha inhibitors." Proposed heading wording:

	• "Secukinumab is more costly and less effective than biosimilar TNF-alpha inhibitors" Proposed clarification in subsequent text: • "In analyses that assume a single efficacy estimate and the costs of biosimilar adalimumab for all TNF-alpha inhibitors, secukinumab is more costly and less effective than TNF-alpha inhibitors. Secukinumab is less costly and is more cost-effective versus certain branded TNF-alpha inhibitors i.e. golimumab and certolizumab pegol". <u>Page 15</u> Current wording: • "The committee did not consider the difference in QALYs to be minimal and noted in most analyses the costs of secukinumab were also higher than TNF-alpha inhibitors." Proposed wording: • "The committee did not consider the difference in QALYs to be minimal and noted that in analyses where the cost of biosimilar adalimumab is assumed for all TNF-alpha inhibitors, the costs of secukinumab were also higher than TNF-alpha inhibitors." <u>Page 16</u> Current wording: • "The costs for secukinumab are generally higher than for TNF-alpha inhibitors." Proposed wording: • "The costs for secukinumab are higher than for biosimilar TNF-alpha inhibitors, such as adalimumab and etanercept, but lower than branded TNF-alpha inhibitors i.e. golimumab and certolizumab pegol."
5	**Second-line analyses** **Novartis comment:** The Novartis model presented results in patients with and without prior exposure to tumour necrosis factor-alpha inhibitors (tumour necrosis factor-experienced, or 2nd line, and tumour necrosis factor-naïve, or 1st line) based on the subgroups in PREVENT. A primary cost-effectiveness analysis was presented for tumour

	necrosis factor-naïve patients (informed by the network meta-analysis), and a secondary cost-effectiveness analysis was presented for tumour necrosis factor-experienced patients (informed by PREVENT data) (Section 3.8 of the Company Submission). Inclusion criteria for the PREVENT trial included the following: • Patients who had been on a tumour necrosis factor-alpha inhibitor (not more than one) had to have experienced an inadequate response to previous or current treatment given at an approved dose for at least 3 months prior to randomisation, or had been intolerant to at least one administration of an anti-tumour necrosis factor-alpha agent. The cost-effectiveness analysis for the second-line population therefore included both individuals who had responded inadequately to tumour necrosis factor-alpha inhibitors and those who were intolerant to at least one dose of a tumour necrosis factor-alpha inhibitor. **Requested amendments:** <u>Page 12:</u> Current wording: • "The company model only included the population in PREVENT who had not had TNF-alpha inhibitors before. The model therefore related only to first-line use of secukinumab. No base-case analysis for the subgroup who cannot have TNF-alpha inhibitors or whose disease responded inadequately to these was presented by the company." Proposed wording: • "The company model included a primary analysis considering the population in PREVENT who had not had TNF-alpha inhibitor before, and a secondary analysis considering the population in PREVENT who had received one prior TNF-alpha inhibitor". <u>Page 16</u> Current wording: • "[The committee] noted that it had only been presented with cost-effectiveness estimates for secukinumab compared with conventional care for the whole population, but considered that secukinumab was likely to be a cost-effective use of NHS resources for people who cannot have TNF-alpha inhibitors. There were no data to determine if these results would be

	different in the subgroup of people who cannot have TNF-alpha inhibitors or whose condition had not responded to a TNF-alpha inhibitor." Proposed wording: • "[The committee] noted that it had only been presented with cost-effectiveness estimates for secukinumab compared with conventional care for the full second line (biologic-experienced) population; no subgroup analysis was presented in people who are contraindicated for, or who cannot have, TNF-alpha inhibitors. The Committee considered that secukinumab was likely to be a cost-effective use of NHS resources for people who cannot have TNF-alpha inhibitors. There were no data to determine if these results would be different in the subgroup of people who cannot have TNF-alpha inhibitors versus the subgroup whose condition had not responded to a TNF-alpha inhibitor."
6	**Company model** **Novartis comment:** In the company submission, the Novartis model considered each individual tumour necrosis factor-alpha inhibitor as a separate treatment option. Following a clarification question from the Evidence Review Group, an additional scenario was provided where a single tumour necrosis factor-alpha inhibitor comparator was included, and a weighted average drug cost was generated based on confidential market share information. **Requested amendments:** <u>Page 12</u> Current wording: • "The company used an average of confidential market share information to cost TNF-alpha inhibitors. It used a single comparator to reflect the effect of TNF-alpha inhibitors as a drug class, and when considering the effect of subsequent treatment with a TNF-alpha inhibitor in the economic model". Proposed wording: • "In the company base-case, each TNF-alpha inhibitor was considered as a separate treatment option. Following a request from the ERG, a scenario was provided in which the company used an average of confidential market share information to cost TNF-alpha inhibitors and a single comparator was used to reflect the effect of TNF-alpha inhibitors as a drug

	class, and when considering the effect of subsequent treatment with a TNF-alpha inhibitor in the economic model".
7	**Patients for whom secukinumab may be the most suitable first-line choice** **Novartis comment:** We agree with the statements on Page 7 that "for disease that has had an inadequate response to TNF-alpha inhibitors, it is preferable to try a new treatment option with an alternative mechanism of action" and that "secukinumab is more effective than TNF-alpha inhibitors for treating psoriasis." We also understand from clinical experts that there are several reasons why first-line treatment with secukinumab may be the right choice for a patient, including: • its suitability for patients with multiple sclerosis or tuberculosis • its safety profile – in randomised controlled trials and in the real-world setting secukinumab has consistently demonstrated a safety profile with very low infection and cancer risk (3) • its administration frequency – monthly administration of secukinumab may be preferential for some patients.
8	**Biosimilar terminology** **Requested amendments:** <u>Page 7</u> Current wording: • "given the extensive clinical experience with TNF-alpha inhibitors and the lower price of generic versions now available". Proposed wording: • "given the extensive clinical experience with TNF-alpha inhibitors and the lower price of biosimilar versions now available".

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Secukinumab for treating non-radiographic axial spondyloarthritis [ID1419]

Consultation on the appraisal consultation document – deadline for comments 5pm on Tuesday 20 April 2021 **email:** NICE DOCS

References

1. National Institute for Health and Care Excellence. TA383: TNF-alpha inhibitors for ankylosing spondylitis and non-radiographic axial spondyloarthritis. Available at: https://www.nice.org.uk/guidance/ta383/chapter/1-Recommendations (last accessed 12th April 2021). 2016.
2. National Institute for Health and Care Excellence. TA497: Golimumab for treating non-radiographic axial spondyloarthritis. Available at: https://www.nice.org.uk/guidance/ta497/chapter/1-Recommendations (last accessed 12th April 2021). 2018.
3. European Medicines Agency. Secukinumab Summary of Product Characteristics. Available at: https://www.ema.europa.eu/documents/product-information/cosentyx-epar-product-information_en.pdf (last accessed 12th April 2021).

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Disclosure Please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry.	None
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	Do not paste other tables into this table, because your comments could get lost – type directly into this table.
Section 3.3 Positioning of secukinumab	UCB agrees with the opinion of the clinical expert presented at the committee meeting. It is not ideal to cycle people with axSpA through TNF inhibitors when they have achieved inadequate response to a previous TNF inhibitor. The ERG on this appraisal favoured using assumptions on future TNF efficacy in line with TA383. These analyses use data from people with rad-axSpA in the DANBIO registry (Glintborg et al. 2013). This registry shows a marked decrease in the efficacy of TNF inhibitors given in sequence. Glintborg et al. 2013 analysed patients who had both 3 and 6 month BASDAI50 data, which excludes patients who have primary non-response (a more favourable subgroup than all patients with inadequate response), and found that median time to drug discontinuation on second line TNF inhibitors was reduced from 3.1 to 1.6 years and that, in patients who switched TNF inhibitors, first line BASDAI50 response was 54% while second line response was only 37% and third line response was 30%. In people with axSpA whose axSpA does not respond to TNF inhibitor treatment within the first 3 to 6 months, response rates on second line TNF inhibitors would be expected to be lower. These DANBIO data support the clinical expert's position that patients who respond inadequately to first-line TNF inhibitors should be tried on treatments with a different mechanism of action such as IL-17s rather than additional TNF inhibitors.
Section 3.10 Cost of TNF-inhibitors as a drug class	Given the low price of adalimumab biosimilar, UCB agrees with clinical opinion stating that adalimumab biosimilar is likely to be the first line biologic of choice. Given heterogeneity in the patient population, setting price assuming that 100% of patients would take biosimilar adalimumab at 1st line is inappropriate. A more appropriate assumption should be based on the goals and performance of the NHSE framework pricing agreement on biosimilar adalimumab. From October 2018 to May 2019, the share of biosimilar adalimumab as first or second biologic across a wide number of indications increased to 63%. The goal of the NHSE framework was to increase this to 80%. A value of 80% should be considered a natural cap on adalimumab market share at first line. This necessarily means that biosimilar adalimumab will not be the treatment of choice for most new second line patients. UCB rejects the assumption that 1st line treatment costs should represent a 100% market share for biosimilar adalimumab, as this biases the analysis substantially in favour of TNF inhibitors. At a minimum, this assumption should be tested in sensitivity analyses. In TA383, NICE analysed TNF inhibitors as being of equivalent efficacy, but also acknowledged that some treatments are better for different patient profiles and that choice of 1st line biologic should be driven by the appropriateness of the therapy to the patient. Adalimumab will not be the most suitable treatment for all patients.
Section 3.10 Etanercept as preferred 2nd line TNF	As in the above point, costing all TNF inhibitors using only one member of the class biases the analysis in favour of TNF inhibitors. Given prescribers should first consider which treatment is most appropriate for patients, cost of the lowest cost biosimilar should not be the only driver of market share calculations. Moreover, etanercept, as noted by the clinical expert, is contraindicated in patients with uveitis, and some patients are contraindicated for TNF inhibitors, in general. It is also the case that patients should be given some voice in their choice of treatment, and many patients are more comfortable with less frequent injections. Etanercept has more frequent injections than other TNF inhibitors. Market data at 2nd line is likely to be more appropriate than assuming 100% etanercept costs.

Insert extra rows as needed

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Role	Medicines Team at NICE
Other role	
Organisation	
Location	
Conflict	
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Comments on the ACD:	
This comment doesn't relate specifically to this TA but is something I picked up on when reviewing it. On checking NG65 on Spondyloarthritis in over 16s (to see where the info on which TNF-alpha inhibitors are recommended for axial spondyloarthritis came from) I could not see any recommendations relating to using golimumab for non-radiographic axial spondyloarthritis. The only rec in that guideline(1.4.3) appears to relate to treating severe active ankylosing spondylitis. However, on searching the NICE website I can see there is a TA for golimumab for non-radiographic axial spondyloarthritis (TA 497). Does TA 497 need incorporating into NG65? Assume this TA when published will also be incorporated into NG65?	