National Institute for Health and Care Excellence

Health Technology Evaluation

Secukinumab for treating moderate to severe hidradenitis suppurativa [ID4039]
Response to stakeholder organisation comments on the draft remit and draft scope

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Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Novartis	Novartis agrees that the proposed evaluation is appropriate. Given the lack of licensed treatment options available to patients with moderate-to-severe hidradenitis suppurativa (HS) for whom adalimumab is contraindicated or unsuitable, including second-line for those who have failed to respond to prior adalimumab treatment, there is a clear need to evaluate a licensed alternative therapy for these patients. Thus, Novartis welcomes an evaluation of its technology (secukinumab) and considers the proposed evaluation route (i.e., single technology appraisal) appropriate.	Thank you for your comment. NICE has scheduled this topic into its work programme. No action required.
	British Association of Dermatologists	A single technology appraisal is appropriate.	Thank you for your comment. NICE has scheduled this topic into its work programme. No action required.

Section	Stakeholder	Comments [sic]	Action
Wording	Novartis	Novartis considers the wording of the remit to be appropriate.	Thank you for your comment. No action required.
	British Association of Dermatologists	The wording is appropriate.	Thank you for your comment. No action required.
Timing issues	Novartis	Without active treatment, HS is a progressive, debilitating disease which negatively impacts the quality of life of patients and carers.[1] Additionally, management of uncontrolled HS is a significant burden to healthcare systems because of the high costs associated with informal care and surgery.[2, 3] As such, there is an urgent need for additional licensed, pharmacological therapies effective at treating HS, with a tolerable safety profile. We therefore believe that timely NICE guidance for secukinumab would be valuable to the NHS. 1. Kouris A, Platsidaki E, Christodoulou C, et al. Quality of Life and Psychosocial Implications in Patients with Hidradenitis Suppurativa. Dermatology 2016;232:687-691. 2. Frings VG, Schöffski O, Goebeler M, et al. Economic analysis of the costs associated with Hidradenitis suppurativa at a German University Hospital. PLoS One 2021;16:e0255560. 3. Gáspár K, Hunor Gergely L, Jenei B, et al. Resource utilization, work productivity and costs in patients with hidradenitis suppurativa: a cost-of-illness study. Expert Rev Pharmacoecon Outcomes Res 2021:1-10.	Thank you for your comment. NICE has scheduled this topic into its work programme. No action required.
	British Association of Dermatologists	High.	Thank you for your comment. NICE has scheduled this topic into its work programme. No action required.

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Additional comments on the draft remit	British Association of Dermatologists	There is a high level of urgency because hidradenitis suppurativa (HS) is a relatively common condition for which there is currently only one licensed and NICE-approved therapy which quite often is insufficient. Access to infliximab is very limited, despite being recommended in BAD guidelines (https://onlinelibrary.wiley.com/doi/10.1111/bjd.17537), because it has not received NICE approval due to insufficient RCT evidence.	Thank you for your comment. NICE has scheduled this topic into its work programme. No action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Novartis	Novartis agree that the background information provided accurately describes the current treatment pathway for patients with HS in England and Wales.	Thank you for your comments. No action required.
	British Association of Dermatologists	Two changes to recommend: (1) "... leads to the formation of pus-filled abscesses which can become infected" - infection is not usually demonstrable and the issue is more inflammatory in nature. (2) "These are painful and can cause itching, redness, burning, excessive sweating..." Best to omit "excessive sweating" because it is not a specific feature of HS.	Thank you for your comments. The following text has been removed: 1) 'which can become infected'; 2) 'excessive sweating'.
Population	Novartis	The anticipated license wording for secukinumab in this indication is "[redacted]". Therefore, Novartis considers the population stated in the draft scope to be appropriate.	Thank you for your comments. No action required.

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	British Association of Dermatologists	Yes.	Thank you for your comments. No action required.
Subgroups	Novartis	Secukinumab is not anticipated to demonstrate differential clinical efficacy in any specific subgroups. However, given the availability of a biosimilar for adalimumab, secukinumab is anticipated to be cost effective in HS patients for whom adalimumab is contraindicated or unsuitable, including those who have failed to respond to prior adalimumab treatment, in line with the anticipated positioning of secukinumab in the clinical care pathway for HS on the NHS.	Thank you for your comments. 'People who have failed to respond to prior adalimumab treatment' has been added as a relevant subgroup.
	British Association of Dermatologists	No, we do not currently have agreed sub-phenotypes of HS or specific sub-populations who should be considered separately.	Thank you for your comments. No action required.
Comparators	Novartis	Given the recommendation by NICE for the use of adalimumab in HS (TA392)[4] and the availability of a biosimilar for adalimumab, secukinumab is anticipated to be positioned in the UK for patients in whom adalimumab is contraindicated or otherwise unsuitable, including those who have failed to respond to prior adalimumab treatment. Therefore, adalimumab does not represent a relevant comparator given the anticipated UK positioning for secukinumab. Furthermore, Novartis agrees that infliximab does not represent a comparator given the NHS England Clinical Commissioning Policy cited a lack of evidence for its use in treating HS and stated that it should not routinely be commissioned.[5] Therefore, since there are currently no therapies recommended for use at the anticipated positioning for secukinumab, HS patients at the relevant point in the treatment pathway are expected to be receiving no active therapy currently. As such, best supportive care (BSC) is anticipated to represent the sole comparator relevant to the anticipated positioning.	Thank you for your comments. As noted, adalimumab is recommended by NICE for the population relevant to this scope (adults with moderate to severe hidradenitis suppurative). Therefore, adalimumab has been retained as a comparator for the scope.

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		4. National Institute of Health and Care Excellence (NICE). Adalimumab for treating moderate to severe hidradenitis suppurativa (TA392). Available at: https://www.nice.org.uk/guidance/ta392. Date accessed: 05 July 2022. 5. NHS England. Clinical Commissioning Policy: Infliximab for the treatment of hidradenitis suppurativa (2016). Available at: https://www.england.nhs.uk/wp-content/uploads/2018/07/Infliximab-for-the-treatment-of-hidradenitis-suppurativa.pdf. Date accessed: 29 July 2022.	As suggested, infliximab is not included as a relevant comparator in this indication.
	British Association of Dermatologists	Yes, provided adalimumab also includes its biosimilars. It should be noted that best supportive care is difficult to define (perhaps doxycycline should be considered here) and is insufficient to prevent disease progression in those with moderate-to-severe HS, allowing progressive scarring to occur.	Thank you for your comments. The availability and cost of biosimilars will also be taken into account. The scope is intended to provide a top-line overview of the comparators and therefore best supportive care is not defined further, but will consider this during the appraisal.
Outcomes	Novartis	Novartis considers the outcomes listed to be pertinent to the evaluation of secukinumab and reflect outcomes of importance to HS patients, the people who care for them and the healthcare professionals who treat them.[6] 6. Thorlacius L, Ingram JR, Villumsen B, et al. A core domain set for hidradenitis suppurativa trial outcomes: an international Delphi process. The British journal of dermatology 2018;179:642-650.	Thank you for your comments. No action required.

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	British Association of Dermatologists	The HIdradenitis SuppuraTiva cORe outcomes set International Collaboration (HISTORIC) has defined six core outcome domains to measure in HS trials: pain, health-related quality of life, physical signs, global assessment (patient & physician), disease progression (flare frequency/time to recurrence), and other symptoms (drainage & fatigue) (Thorlacius *et al.* 2018 https://pubmed.ncbi.nlm.nih.gov/29654696/).	Thank you for your comments. The list of outcomes has been updated to include disease progression. Please note that the list of outcomes provided is not intended to be exhaustive.
Equality	Novartis	As noted in the draft scope, the incidence of HS is higher in people of African-Caribbean family background as compared with people of European family background. No equality issues are foreseen if secukinumab were to be recommended for use for all patients at the anticipated positioning.	Thank you for your comments. These points have been added to the equality impact assessment form. The committee will consider equality issues during the appraisal.
	British Association of Dermatologists	Probable higher incidence in people of Afro-Caribbean family background has been correctly identified. Please bear in mind that peak prevalence (2%) is in females of child-bearing age.	Thank you for your comments. These points have been added to the equality impact assessment form. The committee will consider equality issues during the appraisal.
	Novartis	No comments.	No action required.

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Other considerations	British Association of Dermatologists	Prevention of disease progression in HS is important because it is a scarring condition. The scarring limits function, which in turn limits ability to work and study. Reversal of scarring may require extensive surgery, for example axillary surgery healing times are about 3 months for wide excision and for the groin and buttocks may exceed 6 months.	Thank you for your comments. The background section of the scope has been updated to note that scarring can limit function and require surgery to reverse.
Questions for consultation	Novartis	**Are there different treatments for moderate or severe hidradenitis suppurativa?** No, it is anticipated that patients with moderate HS will receive the same clinical treatment in UK clinical practice as patients with severe HS. This similarity in treatment pathway is underscored by the NICE recommendation for adalimumab in moderate-to-severe HS (TA392).[4] **Should oral antibiotics, dapsone, retinoids, TNF-inhibitors (other than adalimumab) or surgery be included as comparators?** Given the anticipated positioning of secukinumab, it is expected that the relevant patient population will currently be receiving BSC, which is expected to be heterogenous with no established standard of care in place in typical clinical practice (see question below). At the anticipated positioning, it is expected that patients with HS will have already failed to respond to conventional systemic therapies such as oral antibiotics. Regarding TNF-alpha inhibitors other than adalimumab, these are not established NHS practice, given the availability of licensed adalimumab and the NHSE specialised commissioning policy stating that infliximab will not be routinely commissioned.[5] As such, systemic therapies and TNF-alpha inhibitors other than adalimumab do not represent relevant comparators, in line with the scope for TA392.[4]	Thank you for your comments. The points will be considered further during the appraisal. No action required to update the scope.

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		As noted in the draft scope and below, surgery may be considered where medical treatment is insufficient to control HS, or in combination with pharmacological treatment.[7] As such, surgery constitutes an important component of BSC, but it does not represent an alternative or exclusive comparative treatment option. Therefore, Novartis do not consider surgery alone to be a relevant comparator in this appraisal. **What does best supportive care for moderate to severe hidradenitis suppurativa consist of?** Given that there are no active treatments available for the population of interest based on the anticipated positioning for secukinumab, it is expected that the goal of BSC would be to treat acute flare ups of HS rather than to control the disease or to prevent its recurrence. In line with BAD guidelines, BSC is expected to comprise (1) surgical interventions, such as simple local incision and drainage, and intra-lesion steroid injections, and; (2) non-surgical interventions, such as antiseptic therapy, wound care, systemic antibiotics and analgesia.[8] **Would secukinumab be a candidate for managed access?** Given the availability of direct evidence from two large, identically designed, head-to-head comparison trials (SUNSHINE and SUNRISE, each of which recruited just over 540 patients) of secukinumab versus placebo,[9, 10] and since secukinumab is already licensed, approved by NICE and in widespread use within the NHS for multiple other indications, Novartis do not consider it appropriate for secukinumab to be recommended through managed access. **Do you consider secukinumab to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?** Introduction of a licensed therapy that provides an alternative to adalimumab and a different mechanism of action would represent a step-change in the	

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		management of HS. Novartis considers that secukinumab will be of significant benefit to HS patients for whom adalimumab is contraindicated or unsuitable, given the lack of available licensed treatments at the anticipated positioning for secukinumab. **Do you consider that the use of secukinumab can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.** Systemic comorbidities of HS reported in the peer-reviewed literature include axial spondyloarthritis and psoriatic arthritis.[4, 11-13] Since these are licensed indications for secukinumab with optimised NICE recommendations, the introduction of secukinumab as a treatment for HS could have benefits for patients with these concomitant comorbidities.[11, 13] These benefits will not be captured within the cost per QALY analysis of this appraisal, which captures benefits directly associated with the treatment of HS only. **Would it be appropriate to use the cost-comparison methodology for this topic? Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?** Given that secukinumab is being positioned for a population of HS patients for whom BSC is the relevant comparator, Novartis considers it inappropriate to conduct a cost-comparison because of the differential efficacy between secukinumab and BSC. However, although adalimumab is not considered a relevant comparator at the anticipated positioning of secukinumab, the prior NICE recommendation of adalimumab in HS provides a useful decision-making framework for the use of secukinumab in HS. **Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?**	

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		The primary endpoint, Hidradenitis Suppurativa Clinical Response (HiSCR), in the SUNSHINE and SUNRISE trials was developed and validated in the context of the development program of adalimumab in HS. The HiSCR is considered to be adequately described and validated for use as the primary endpoint in pivotal studies and has already been the basis for the EMA approval of adalimumab for treating moderate-to-severe HS.[14] Additionally, HiSCR reflects important domains in HS identified by the scientific community as being of most importance to patients.[6] **Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?** No further evidence has been identified. 4. National Institute of Health and Care Excellence (NICE). Adalimumab for treating moderate to severe hidradenitis suppurativa (TA392). Available at: https://www.nice.org.uk/guidance/ta392. Date accessed: 05 July 2022. 5. NHS England. Clinical Commissioning Policy: Infliximab for the treatment of hidradenitis suppurativa (2016). Available at: https://www.england.nhs.uk/wp-content/uploads/2018/07/Infliximab-for-the-treatment-of-hidradenitis-suppurativa.pdf. Date accessed: 29 July 2022. 6. Thorlacius L, Ingram JR, Villumsen B, et al. A core domain set for hidradenitis suppurativa trial outcomes: an international Delphi process. The British journal of dermatology 2018;179:642-650. 7. Zouboulis CC, Desai N, Emtestam L, et al. European S1 guideline for the treatment of hidradenitis suppurativa/acne inversa. J Eur Acad Dermatol Venereol 2015;29:619-44. 8. Ingram JR, Collier F, Brown D, et al. British Association of Dermatologists guidelines for the management of hidradenitis suppurativa (acne inversa) 2018. British Journal of Dermatology 2019;180:1009-1017.	

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		9. ClinicalTrials.gov. This is a Study of Efficacy and Safety of Two Secukinumab Dose Regimens in Subjects With Moderate to Severe Hidradenitis Suppurativa (HS). (SUNSHINE). 10. ClinicalTrials.gov. Study of Efficacy and Safety of Two Secukinumab Dose Regimens in Subjects With Moderate to Severe Hidradenitis Suppurativa (HS) (SUNRISE). 11. Fauconier M, Reguiai Z, Barbe C, et al. Association between hidradenitis suppurativa and spondyloarthritis. Joint Bone Spine 2018;85:593-597. 12. Richette P, Molto A, Viguier M, et al. Hidradenitis Suppurativa Associated with Spondyloarthritis — Results from a Multicenter National Prospective Study. The Journal of Rheumatology 2014;41:490. 13. Schneeweiss MC, Kim SC, Schneeweiss S, et al. Risk of Inflammatory Arthritis After a New Diagnosis of Hidradenitis Suppurativa. JAMA Dermatol 2020;156:342-345. 14. EMA. Humira (Adalimumab) EPAR (last updated September 2021)	
	British Association of Dermatologists	**What is the current treatment pathway for people with moderate to severe hidradenitis suppurativa?** The pathway follows the BAD guidelines 2018 (https://onlinelibrary.wiley.com/doi/10.1111/bjd.17537), with three main differences: (1) Dapsone is being used less and less because, while it has benefit in relatively mild disease, it is rarely sufficiently effective as monotherapy for moderate-to-severe disease. (2) Infliximab is not available in England, despite featuring in the guidelines. (3) Adalimumab primary or secondary failure is relatively common and co-treatments such as long-term antibiotics are being added to maintain disease control in the absence of other treatment options.	Thank you for your comments. The points will be considered further during the appraisal. No action required to update the scope.

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		Where do you consider secukinumab will fit into the existing care pathway for hidradenitis suppurativa? Immediately after adalimumab, in the context that adalimumab biosimilars have reduced the price considerably. **Are there different treatments for moderate or severe hidradenitis suppurativa?** The treatments are those covered by the BAD guidelines (https://onlinelibrary.wiley.com/doi/10.1111/bjd.17537). In the past, adalimumab has been used more for severe disease, however, it is increasingly used for moderate disease in order to prevent disease progression, including scarring. **Is infliximab considered to be established clinical practice in the NHS for treating hidradenitis suppurativa?** Infliximab was established clinical practice for HS previously, but lack of access in England means it is rarely used now. **Should oral antibiotics, dapsone, retinoids, TNF-inhibitors (other than adalimumab) or surgery be included as comparators?** No, oral therapies and surgery are used as concomitant treatments, rather than in place of biologic therapy. There are insufficent data for anti-TNF inhibitors for HS other than adalimumab. **Are biosimilars likely to be established clinical practice for the treatment of hidradenitis suppurativa?** Yes – adalimumab.	

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		Would secukinumab be a candidate for managed access? Possibly, however, the phase III trial data coming through should provide sufficient evidence. **Do you consider secukinumab to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?** Secukinumab will provide a step-change in HS management, as the first anti-IL17 therapy available for HS and a much needed alternative biologic for the quite high proportion of HS patients exhibiting adalimumab primary or secondary failure. Patients' expectations now exceed the 50% improvement in inflammatory lesions denoted by the HiSCR trial endpoint and only 50% of HS patients reached even this endpoint in the adalimumab PIONEER studies (Kimball *et al.* 2016, https://pubmed.ncbi.nlm.nih.gov/27518661/). **Do you consider that the use of secukinumab can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** Patients report that pain is a key part of living with HS. While some of the functional impact of pain is included in QALY calculations, the burden of living with either chronic pain, or unpredictable episodic pain associated with flares, should not be underestimated. Pain scores of 10/10 (worst pain imaginable) are quite often reported in HS. **Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.** Important to include pain numerical rating scale/visual analogue scale data.	

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Additional comments on the draft scope	Novartis	Novartis suggest adding the following wording to 'The technology' section: "Secukinumab (Cosentyx, Novartis) is recombinant high-affinity fully human monoclonal immunoglobulin G1/kappa antibody that selectively binds to and neutralises the proinflammatory cytokine IL-17A. IL-17A is the central cytokine in multiple autoimmune and inflammatory processes, including HS."	Thank you for your comments. Currently, NICE does not typically include the mechanism of action of technologies within a scope, therefore no action has been taken here.
	British Association of Dermatologists	It should be noted that successfully preventing disease progression will have large economic benefits in the HS population which is nearly all of working age. Uncontrolled disease leads to high healthcare resource utilisation in the form of A&E attendances, need for surgery and prolonged wound healing times, and the burden of comorbid health problems such as depression, anxiety and cardiovascular disease.	Thank you for your comments. It is anticipated that the economic benefits of preventing disease progression will be explore in detail during the appraisal process. No changes required in the scope.

The following stakeholders indicated that they had no comments on the draft remit and/or the draft scope

AbbVie Ltd.