National Institute for Health and Care Excellence

Single Technology Appraisal (STA/MTA)
Secukinumab for treating moderate to severe plaque psoriasis

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

Comment 1: the draft remit

Section	Consultees	Comments	Action
Appropriateness	Novartis UK	Appropriate	Comments noted. No action required.
	AbbVie Ltd	No comment	Comments noted. No action required.
	Janssen	Janssen agrees that it is appropriate to refer this topic to NICE for appraisal.	Comments noted. No action required.
	Psoriasis and Psoriatic Arthritis Alliance	Cytokine IL-17 has been identified, as having a critical role in the pathogenesis of psoriasis and psoriatic arthritis. Therefore, it would be entirely appropriate for secukinumab a targeted anti-IL-17A agent, to be referred for appraisal.	Comments noted. No action required.
	British Association of Dermatologists/Royal College of Physicians	Yes.	Comments noted. No action required.
Wording	Novartis UK	Agree	Comments noted. No action required.
	AbbVie Ltd	No comment	Comments noted. No action required.

Section	Consultees	Comments	Action
	Janssen	No comment	Comments noted. No action required.
	Psoriasis and Psoriatic Arthritis Alliance	The wording appears to fit with current comparators, but without exact UK marketing authorisation it is difficult to be fully sure.	Comments noted. No action required.

Section	Consultees	Comments	Action
Timing Issues	Novartis UK	Due to the unmet need in treating moderate-severe plaque psoriasis (see below) it is important that guidance is provided for this technology as soon as possible following marketing authorisation. Current NICE approved treatments for moderate to severe psoriasis are not effective in all patients and many patients remain symptomatic despite intervention with biologic therapies (1). Moreover, it is now understood that, in those that do respond, the efficacy of biologic intervention diminishes over time (2). A recent publication from the Danish registry (DERMBIO) demonstrated that the 4-year drug survival is in the range of 40% for etanercept or adalimumab, the two most commonly used biologic therapies in the UK (2). Therefore, there is currently an unmet need in patients that may have inadequate response to existing treatments or experienced loss of efficacy with existing treatments. Current biologic therapies for psoriasis include only two mechanisms of action (anti-TNFa antibodies and an anti-IL12/23 antibody) and so therapies with a new mechanism of action are needed. It is beneficial to give people with psoriasis access to this technology which has a novel mechanism of action (anti-IL17A antibody). To this regard, it will be important to provide guidance to the NHS as close as possible to marketing authorisation so that clinicians and patients have an additional therapeutic option as soon as possible. (1). Reich K, Burden AD, Eaton JN, Hawkins NS. Efficacy of biologics in the treatment of moderate to severe psoriasis: a network meta-analysis of randomized controlled trials. Br J Dermatol. 2012; 166:179-88. (2). Gniadecki R, Kragballe T, Dam TN, Skov L. Comparison of drug survival rates for adalimumab, etanercept and infliximab in patients with psoriasis vulgaris. *Br J Dermatol.* 2011; **164**:1091–6.	Comments noted. No action required.

Section	Consultees	Comments	Action
	AbbVie Ltd	No comment	Comments noted. No action required.
	Janssen	No comment	Comments noted. No action required.
	Psoriasis and Psoriatic Arthritis Alliance	Psoriasis has a number of recommended agents of similar class. For patients who fail these drugs and have uncontrolled disease an alternative treatment is of utmost urgency, but for the population described it is less urgent.	Comments noted. No action required.
Additional comments on the draft remit	Novartis UK	None	Comments noted. No action required.
	AbbVie Ltd	None	Comments noted. No action required.
	Janssen	No additional comment	Comments noted. No action required.
	Psoriasis and Psoriatic Arthritis Alliance	There does not appear to a distinction in the age of the population, which will probably be reflected by the licence. However, children have limited access to biologic agents therefore, if evidence exist in that group, it might useful to consider. Particularly if transitioning from paediatric care into adult services and any sequencing issues that arise if other agents have been used within licensed application.	Comments noted. NICE has to appraise technologies within their marketing authorisation, including any stipulations on age in the marketing authorisation.

Section	Consultees	Comments	Action
			Issues around sequencing are likely to be outside the remit of a single technology appraisal.

Comment 2: the draft scope

Section	Consultees	Comments	Action
Background information	Novartis UK	Psoriasis negatively affects people's lives both physically and psychologically. Physical features are often painful and include burning sensations, joint pain, itching and skin soreness. These factors regularly limit people's ability to undertake daily activities and take their toll on psychological health. In fact, the effect of psoriasis on people's health-related quality of life has been shown to be similar to diseases such as cancer, heart disease, arthritis, type 2 diabetes and depression (1,2,3). A number of international studies also confirm that people with more severe forms of psoriasis have a significantly reduced life span (1). This is because they are more likely to suffer from a range of co-morbidities, including obesity, metabolic syndrome, cardiovascular disease, psychiatric illness and cancer (2). Psoriasis often causes serious pain and suffering because of the parts of the body affected. The disease can be extremely painful and difficult to treat when it appears on the hands, feet, nails, scalp and areas where the skin rubs together, such as the underarms. In addition when psoriasis is highly visible, such as on the face and nails, it is a major influencing factor on people's emotional wellbeing (4). People with psoriasis can also endure greater physical disability when areas such as the hands, feet and nails are affected. This includes functional disability related to symptoms such as burning sensations and skin soreness. Additionally patients are at risk of secondary infections. Where there is a prolonged duration of psoriasis there is a risk of joint involvement (5,6). (1). Rapp SR, Feldman SR, Exum ML, Fleischer AB, Jr., Reboussin DM. Psoriasis causes as much disability as other major medical diseases. J Am Acad Dermatol 1999; 41(3 Pt 1):401-7. (2). Guenther L et al. Psoriasis Comorbidities. J Cutan Med Surg. 2009; 13(12) S77-S87 (3). Stern RS, Nijsten T, Feldman SR, Margolis DJ, Rolstad T. Psoriasis Is Common, Carries a	Comments noted. The background section is only intended to provide a brief overview of the disease and its associated management.

Section	Consultees	Comments	Action
		Substantial Burden Even When Not Extensive, and Is Associated with Widespread Treatment Dissatisfaction. J Investig Dermatol Symp Proc 2004; 9(2):136-9 (4). Wozel G. Psoriasis treatment in difficult locations: scalp, nails, and intertriginous areas. Clin Dermatol 2008; 26(5):448-59. (5). Pettey AA, Balkrishnan R, Rapp SR, Fleischer AB, Feldman SR. Patients with palmoplantar psoriasis have more physical disability and discomfort than patients with other forms of psoriasis: Implications for clinical practice. J Am Acad Dermatol 2003; 49(2):271-5 (6). Radtke MA, Langenbruch AK, Schafer I. Nail psoriasis as a severity indicator: results from the PsoReal study. Patient Relat Outcome Meas 2011; 2:1-6 Although at the time of writing, the interim value-based pricing (VBP) framework has yet to be divulged, it may be relevant to include some information regarding the wider societal impact of psoriasis. Several studies have sought to address this issue- 59.3% of patients reported a mean of 26 days of work lost during the preceding year (1). In another study 10% of patients reported 3 or more days of absence in the last 4 weeks (2). Patients with severe disease had a lower probability of being in full-time employment in another analysis (3). As noted in the draft scope, invitation to submit will likely be after January 2014 meaning that should this TA go ahead, it will be subject to the interim VBP process- although further consultation is suggested, it would be helpful to begin to highlight the broader impact of psoriasis in this part of the scoping process, given that it is anticipated that wider societal benefits will be part of the interim VBP process. It should also be highlighted that severe disease may result in hospitalisation- in CG153 the weighted average length of stay per patient per year was found to be 26.6 days. Previous NICE TAs' have used 20 days. A statement to this effect to indicate the clinical/resource impact in people with severe disease should be included.	Following consultation on the proposal for value based assessment, NICE will not yet amend its methods but instead carry out further work before making changes to the way it appraises new medicines and other technologies for use by the NHS. This will be done as part of a wider review of the innovation, evaluation and adoption of new treatments. https://www.nice.org.uk/news/press-and-media/nice-calls-for-a-new-approach-to-managing-the-entry-of-drugs-into-the-nhs

Section	Consultees	Comments	Action
		(1) Finlay AY, Coles EC. The effect of severe psoriasis on the quality of life in 369 patients. Br J Dermatol 1995(132) 236–244 (2) Schmitt JM, Ford DE. Work limitations and productivity loss are associated with health-related quality of life but not with clinical severity in patients with psoriasis. Dermatology 2006 (213)102–110 (3) Horn et al. Association of patient-reported psoriasis severity with income and employment. J Am Acad Dermatol. 2007 Dec; 57(6):963-71	
	AbbVie Ltd	No comment	Comments noted. No action required.
	Janssen	No comment	Comments noted. No action required.
	Psoriasis and Psoriatic Arthritis Alliance	No mention of psoriatic arthritis, particularly as some comparators are also recommended for that. No mention of wider co morbidities, given the awareness rose in the NICE Psoriasis guideline it would be useful to reinforce that awareness at any opportunity of general disease profile.	Comments noted. The background section is only intended to provide a brief overview of the disease and its associated management.
	British Association of Dermatologists/ Royal College of Physicians	We recommend that the background information should make reference to, and detail where relevant, the NICE guidelines for the assessment and management of psoriasis (for example, there are a number of topical treatments mentioned that are not effective or recommended within the CG153).	Comments noted. The background section is only intended to provide a brief overview of the disease and its associated management.
The technology/	Novartis UK	Agree	Comments noted. No action required.

Section	Consultees	Comments	Action
intervention	AbbVie Ltd	AbbVie suggest changing: *"Secukinumab does not currently have a UK marketing authorisation for treating moderate to severe plaque psoriasis. It has been studied in clinical trials compared with placebo or etanercept in adults with moderate to severe psoriasis for whom topical treatment, phototherapy and/or systemic therapy have been inadequately effective,"* to *"Secukinumab does not currently have a UK marketing authorisation for treating moderate to severe plaque psoriasis. It has been studied in clinical trials compared with placebo or etanercept in adults with moderate to severe psoriasis for whom topical treatment, phototherapy and/or systemic therapy* ***(including other biological therapies)*** *have been inadequately effective."* AbbVie suggest this additional wording more accurately reflects the studied trial population(s).	Comments noted. The manufacturer confirmed that a small proportion of the population had previously received biologics. It was agreed at the workshop that the existing wording adequately reflected the study population, and to include patients with previous treatment with biologics as a sub-group, if the evidence allows.
	Janssen	No comment	Comments noted. No action required.
	Psoriasis and Psoriatic Arthritis Alliance	It appears to match trial data	Comments noted. No action required.
	British Association of Dermatologists/ Royal College of Physicians	Yes.	Comments noted. No action required.

Section	Consultees	Comments	Action
Population	Novartis UK	The study populations were patients with moderate to severe chronic plaque-type psoriasis that is poorly controlled by topical treatments **and / or** phototherapy **and / or** previous systemic therapy.	Comments noted. Scoping workshop attendees agreed that the existing population wording accurately reflected the likely population to be covered by the marketing authorisation.
	AbbVie Ltd	AbbVie suggest adding as a sub-group of interest: *"People with moderate to severe plaque psoriasis for whom other systemic therapies including ciclosporin, methotrexate and phototherapy with or without psoralen* ***or other biological therapies*** *have been inadequately effective, not tolerated or contraindicated."* This is because AbbVie consider that it is appropriate to look at the clinical and cost-effectiveness of secukinumab in those patients who have previously had an inadequate response with, been intolerant or contraindicated to other biological therapies as it is not clear at this stage where it will be positioned.	Comments noted. The manufacturer confirmed that a small proportion of the population had previously received biologics. It was agreed to include patients with previous treatment with biologics as a sub-group, if the evidence allows.
	Janssen	No comment	Comments noted. No action required.
	Psoriasis and Psoriatic Arthritis Alliance	Matches trial population	Comments noted. No action required.
	British Association of Dermatologists/ Royal College of Physicians	Yes.	Comments noted. No action required.

Section	Consultees	Comments	Action
Comparators	Novartis UK	Best supportive care should also be included as a comparator. Patients who are contraindicated or intolerant to existing biologic therapy will likely be assigned best supportive care, in the absence of any biologic therapeutic alternative. In CG153, second line biologic therapy was compared to best supportive care. It should also be noted that the established cost-effectiveness modelling approach defined from TA103 onwards (and used in CG153) uses best supportive care as the absorbing health state. Therefore it is important that supportive care is included as a comparator. Biosimilars cannot be included as comparators as they are not established treatments, none are currently available, and are not expected to be until 2015 at the earliest. The 2013 methods guide states that amongst the factors considered regarding the choice of appropriate comparator(s) are 'established NHS practice in England' and the 'licensing status of the comparator'. At the time of writing, the only biosimilar products with EMA approval are infliximab biosimilars. Current understanding is that there is no imminent launch expected of an infliximab biosimilar until at least Feb 2015 due to a patent extension that covers the majority of the EU, including the UK. It therefore follows that biosimilars cannot be considered as appropriate comparators as they will not represent established practice in the NHS in England. Furthermore, there will be no clarity on price for a significant period, which will limit the feasibility of any comparison with an infliximab biosimilar. In addition, the infliximab originator molecule has limited use in this population (estimated to be less than 10%-data on file). In the interests of issuing timely guidance; the limited use of infliximab in this indication as well as the unavailability of biosimilars highlighted above must be	Comments noted. The comparators section has been updated.

Section	Consultees	Comments	Action
		considered. Therefore biosimilars should not be included as comparators.	
	AbbVie Ltd	AbbVie consider that the appropriate comparator may differ depending on which population secukinumab is studied within. When looking at: *"People with moderate to severe plaque psoriasis for whom other systemic therapies including ciclosporin, methotrexate and phototherapy with or without psoralen have been inadequately effective, not tolerated or contraindicate,"* AbbVie agree that the appropriate comparators are: *"Biologic therapies (including etanercept, infliximab, adalimumab, ustekinumab and biosimilars)"* However, when looking at: *"People with moderate to severe plaque psoriasis for whom other systemic therapies including ciclosporin, methotrexate and phototherapy with or without psoralen* ***or other biological therapies*** *have been inadequately effective, not tolerated or contraindicated,"* AbbVie consider the appropriate comparators are: *"Conventional management strategies excluding the use of biological therapies"* AbbVie suggest that, if biosimilars are to be included as comparators in the proposed or any other future appraisal, the Institute should provide clear guidelines on how biosimilars will be appraised, particularly if there is an absence of trial data on the clinical effectiveness and safety within the specific licensed indication under consideration.	Comments noted. The comparators section has been updated.

Section	Consultees	Comments	Action
	Janssen	Janssen believes that 'best supportive care' remains a relevant comparator since many patients who are eligible for biologic therapy are in fact not receiving one. According to the NICE biologic drug commissioning guide, 18,000 psoriasis patients are estimated to be eligible to receive a biologic drug. (Although the commissioning guide states this is the "estimated number of people with the condition eligible and receiving treatment with biologic drugs", an email communication with NICE confirmed that the 18,000 figure does not necessarily represent a number of psoriasis patients who are actually receiving a biologic therapy.) The nationwide market research commissioned by Janssen suggests less than 9,000 psoriasis patients are currently receiving a biologic therapy, indicating approximately 50% of psoriasis patients who are eligible for a biologic therapy are receiving 'best supportive care' instead.	Comments noted. The comparators section has been updated.
	Merck Sharp and Dohme	MSD believes that the inclusion of biosimilars as comparators is inappropriate because at the time of the final scope being issued biosimilars will not yet be available for use in UK clinical practice (prior to the Remicade patent expiry), will have no clinical data relating to the psoriasis indication to support considerations of clinical effectiveness, and will not have a list price to support considerations of cost-effectiveness.	Comments noted. The comparators section has been updated.
	Psoriasis and Psoriatic Arthritis Alliance	Includes current therapies	Comments noted. No action required.
Outcomes	Novartis UK	Agree	Comments noted. No action required.
	AbbVie Ltd	Yes	Comments noted. No action required.
	Janssen	No comment	Comments noted. No action required.

Section	Consultees	Comments	Action
	Psoriasis and Psoriatic Arthritis Alliance	Benefit to psoriatic arthritis might be useful	Comments noted. It was agreed at the scoping workshop that psoriatic arthritis should not be included as an outcome. It was noted that it was likely that this would have a negligible effect on the cost-effectiveness results.
	British Association of Dermatologists/ Royal College of Physicians	We feel that the outcomes that are being considered are fine, but do not include all the relevant domains that were considered important when evaluating interventions in the CG153. Since these were subject to widespread consultation and agreement, they should be considered. This includes, Physicians Global Assessment (i.e. number who are clear or nearly clear); Patients Global Assessment; impact as it relates to mood (the DLQI does not capture this); impact on psoriatic arthritis; adverse effects including number of withdrawals.	Comments noted. The outcomes currently described in the scope include all of these more detailed outcomes except for psoriatic arthritis. It was agreed at the scoping workshop that psoriatic arthritis should not be included as an outcome. It was noted that it was likely that this would have a negligible effect on the cost-effectiveness results.

Appendix D - NICE's response to consultee and commentator comments on the draft scope and provisional matrix

Section	Consultees	Comments	Action
Economic analysis	Novartis UK	Time horizon will be dependent on the assumptions used in the model- previous TAs have used a 10 year time horizon driven by the assumption of a 20% annual withdrawal rate for all treatments. It may be helpful to note that costs may be considered from a broader perspective than NHS/PSS depending on the nature of the interim value based pricing framework.	Following consultation on the proposal for value based assessment, NICE will not yet amend its methods but instead carry out further work before making changes to the way it appraises new medicines and other technologies for use by the NHS. This will be done as part of a wider review of the innovation, evaluation and adoption of new treatments. https://www.nice.org.uk/news/press-and-media/nice-calls-for-a-new-approach-to-managing-the-entry-of-drugs-into-the-nhs
	AbbVie Ltd	No comment	Comments noted. No action required.
	Janssen	No comment	Comments noted. No action required.
Equality and Diversity	Novartis UK	No comments	Comments noted. No action required.
	AbbVie Ltd	No comment	Comments noted. No action required.
	Janssen	No comment	Comments noted. No action required.

Section	Consultees	Comments	Action
	Psoriasis and Psoriatic Arthritis Alliance	None	Comments noted. No action required.
	British Association of Dermatologists/ Royal College of Physicians	No equality issues.	Comments noted. No action required.

Section	Consultees	Comments	Action
Innovation	Novartis UK	The technology is innovative in that it is the first biologic that specifically targets the IL-17A cytokine. Clinical data recently released demonstrates that this technology is highly effective and is a "step-change" in psoriasis management (1) Without knowledge of the interim value based pricing framework, we cannot determine if there are health-related benefits that will be include in the QALY calculation. Under the current process there are no anticipated *significant and substantial* health-related benefits that would not be included in the QALY calculation. (1) Langley, R. et al Secukinumab Compared With Placebo and Etanercept: A Head-to-Head Comparison of Two Biologics in a Phase 3 Study of Moderate-to-Severe Plaque Psoriasis (FIXTURE) EADV, Oct 2013	Comment noted. The potential innovative nature of the technology would be considered as part of the appraisal. Following consultation on the proposal for value based assessment, NICE will not yet amend its methods but instead carry out further work before making changes to the way it appraises new medicines and other technologies for use by the NHS. This will be done as part of a wider review of the innovation, evaluation and adoption of new treatments. https://www.nice.org.uk/news/press-and-media/nice-calls-for-a-new-approach-to-managing-the-entry-of-drugs-into-the-nhs
	AbbVie Ltd	No comment	Comments noted. No action required.
	Janssen	No comment	Comments noted. No action required.

Section	Consultees	Comments	Action
	Psoriasis and Psoriatic Arthritis Alliance	Different target, but not innovative in other respects.	Comment noted. The potential innovative nature of the technology would be considered as part of the appraisal.
Other considerations	Novartis UK	If evidence allows, in addition to the draft remit assessing secukinumab in its' licensed indication, which essentially equates to first line use, 2nd line use could also be considered. There is currently limited advice on which biologic(s) should be used 2nd line. CG153 does give guidance on the cost-effectiveness of the use of a second biologic (by treating the use of biologics as a class-effect). Giving NICE mandated guidance for the use of this technology as a second biologic (with the comparator of best supportive care) would be beneficial in giving clarity of access to second biologic treatments for moderate to severe psoriasis patients in the NHS.	Comments noted. If the evidence allows, the place of secukinumab in a sequence of biologics will be considered. .
	AbbVie Ltd	No comment	Comments noted. No action required.
	Janssen	No comment	Comments noted. No action required.
	British Association of Dermatologists/ Royal College of Physicians	It should be noted, that clear recommendations on the use of PUVA therapy were produced in the CG153; these recommendations state that before offering this treatment to patients with psoriasis other interventions, "including biologics", should be actively considered. The evaluating committee are asked to note this when considering the health economic model used for the cost effectiveness assessment.	Comments noted. This would be considered as part of the appraisal.
Questions for consultation	Novartis UK	We believe the STA process to be appropriate in order for timely guidance to be issued for this area of unmet need and to give patient's access to this therapy.	Comments noted. No action required.

Section	Consultees	Comments	Action
	AbbVie Ltd	If any sequential use recommendations result from the proposed STA of secukinumab in psoriasis, AbbVie consider it would be appropriate for the Institute to consult on the need to review existing appraisals TA103, TA134, TA146 and TA180 relating to currently licensed biologic therapies in psoriasis. Currently, no sequential use recommendations are made in these existing appraisals relating to adalimumab, etanercept, infliximab and ustekinumab use.	Comments noted. Any recommendations impacting on existing recommendations would be considered as part of the appraisal in this area.
	Janssen	No comment	Comments noted. No action required.
	Psoriasis and Psoriatic Arthritis Alliance	Sequencing of drug via identification of patients who are likely responders would be useful. Impact of benefit on psoriatic arthritis, as overall cost benefit and impact on QoL of both aspects as combined score.	Comments noted. If the evidence allows, the place of secukinumab in a sequence of biologics will be considered. It was agreed at the scoping workshop that psoriatic arthritis should not be included as an outcome. It was noted that it was likely that this would have a negligible effect on the cost-effectiveness results.

Section	Consultees	Comments	Action
Additional comments on the draft scope.	Novartis UK	Although it is appreciated that there can be no clear direction given at the moment, it may be helpful if there is discussion during the scoping workshop of which aspects of the scope may be subject to further consultation following the dissemination of the anticipated interim VBP process.	Comments noted. Following consultation on the proposal for value based assessment, NICE will not yet amend its methods but instead carry out further work before making changes to the way it appraises new medicines and other technologies for use by the NHS. This will be done as part of a wider review of the innovation, evaluation and adoption of new treatments. https://www.nice.org.uk/news/press-and-media/nice-calls-for-a-new-approach-to-managing-the-entry-of-drugs-into-the-nhs
	AbbVie Ltd	No comment	Comments noted. No action required.
	Janssen	No additional comment	Comments noted. No action required.

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

Healthcare Improvement Scotland
The Royal College of Nursing
Department of Health
Pfizer feels that the draft remit for the proposed appraisal and the draft scope which has been developed from the draft remit are appropriate.

NATIONAL INSTITUTE FOR HEALTH AVD CARE EXCELLENCE

Single Technology Appraisal (STA)

Secukinumab for treating moderate to severe plaque psoriasis

Response to consultee and commentator comments on the provisional matrix of consultees and commentators (pre-referral)

Version of matrix of consultees and commentators reviewed: Provisional matrix of consultees and commentators sent for consultation					
Summary of comments, action taken, and justification of action:					
	Proposal:	Proposal made by:		Action taken: Removed/Added/Not included/Noted	Justification:
1.	Add British Society for Investigational Dermatology	Novartis		Not included	The BSID's principle function appears to be organising meetings for relevant specialists and they do not appear to engage in consultations.
2.	No manufacturers of biosimilars were listed.	Psoriasis and Psoriatic Arthritis Alliance		Noted	Please see response on page 11 of this document.