NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

MULTIPLE TECHNOLOGY APPRAISAL

Certolizumab pegol and secukinumab for treating active psoriatic arthritis after inadequate response to DMARDs [ID579]

The following documents are made available to the consultees and commentators:

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

2. **Consultee and commentator comments on the Appraisal Consultation Document** from:
   - Novartis
   - UCB
   - AbbVie
   - Celgene
   - Psoriasis Association

There were no comments submitted by the experts or through the NICE website.

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

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Multiple Technology Appraisal

Certolizumab pegol and secukinumab for treating active psoriatic arthritis after inadequate response to DMARDs

Response to consultee, commentator and public comments on the Appraisal Consultation Document (ACD2)

Definitions:

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 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 determination (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, 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.

Comments received from consultees

Consultee	Comment [sic]	Response
UCB	**<u>General comments :</u>** **Reconsideration of recommendations for certolizumab pegol in Subpopulation 1 (biologic naïve with one prior cDMARD) in their guidance to the NHS)** Section 4.2, page 7 of the ACD states that: '*The committee heard from the clinical and patient experts that the psoriatic arthritis population is heterogeneous. Some people's disease responds to the first disease-modifying anti-rheumatic drug (DMARD), whereas some people's disease may respond to a second or a third DMARD. Some people's disease may not respond all.… The committee was aware that the British Society for Rheumatology guidelines also mention that biological therapies (that is, tumour necrosis factor [TNF]-alpha inhibitors) can be considered in people with specific prognostic factors (including 5 or more swollen joints together with elevated C-reactive protein persisting for more than 3 months or structural joint damage caused by disease) when 1 DMARD has not worked*'. Furthermore, in section 4.16, pages 15-16 of the ACD it is stated that: '...*However, the committee was not convinced that the use of biological therapy after 1 DMARD is established clinical practice in the NHS (see section 4.2) and if it is, in which specific group of people it is used*….. *The committee concluded it was unable to recommend certolizumab pegol and secukinumab as treatment options for people with psoriatic arthritis whose disease had not responded adequately to 1 DMARD*'. UCB understands how the Appraisal Committee reached this conclusion and that it was unable to recommend certolizumab pegol in subpopulation 1 (i.e. biologic naïve patients who have not responded adequately to only one cDMARD). However UCB would like to reiterate that: 1. the GRAPPA and EULAR clinical practice guidelines for the management of PsA and their subsequent updates in 2015, as well as the 2012 BSR guidelines (due to be updated in 2017), recommend the use of TNF inhibitors (such as certolizumab pegol) in certain types of patients who have had an inadequate response to only one cDMARD. For example those with	Thank you for your comment. The Committee considered all the evidence submitted, including evidence from clinical trials, patient and clinical experts, the Assessment Group's economic analysis and the companies' submissions. It also carefully considered the comments received from C&Cs in response to the Assessment Report. The committee concluded that certolizumab pegol and secukinumab could not be recommended as treatment options for people with psoriatic arthritis whose disease had not responded adequately to 1 DMARD, as specified in section 4.16 of the final appraisal determination (FAD)

	• predominant axial disease, predominant nail involvement, dactylitis and/or predominant enthesitis; • poor prognostic factors. A summary of these recommendations is provided thereafter. 2. The UK clinical practice is highly guided by recommendations from NICE, which currently restrict the use of TNF inhibitors after inadequate response to 2 cDMARDs, thus evidence on their usage after only 1 cDMARD within the NHS is limited creating a cycle whereby formal audited data on their use is not available. 3. Previous NICE guidance has provided recommendations allowing the use of biologics in a specific subpopulation where no biologics were previously recommended (eg TA340, ustekinumab as treatment option for treating active psoriatic arthritis in adults who had treatment with 1 or more TNF–alpha inhibitors).[5] <u>Treatment management recommendations for use of TNF inhibitors (including certolizumab pegol) in certain types of patients with an inadequate response to only one cDMARD</u> PsA is a heterogeneous disease, associated with multiple and variable clinical features (in terms of both presentation and severity). Patients experience chronic inflammatory peripheral arthritis and may also suffer from skin and nail disease, axial disease, dactylitis and enthesitis. It has been suggested that early intervention in PsA may limit damage to structural joints and produce improvements in pain and/or quality of life. Conventional DMARDs (cDMARDs), used to reduce the immunological over-reactivity seen in PsA, have little evidence to support the inhibition of structural damage progression or efficacy in patients with predominant axial disease or enthesitis. Moreover as noted in TA340 by NICE: '…*conventional management with DMARDs (such as methotrexate) does not appear to provide substantial benefits for joint -related aspects of psoriatic arthritis*.'[5] A synthetic targeted DMARD (apremilast) has also been licensed, although it has shown no significant effect on dactylitis and has no data for the effect on structural damage. TNF inhibitors, including certolizumab pegol, are efficacious and have proven persistent therapeutic benefits in many areas of functional status and HRQoL, although etanercept is not considered as efficacious as other TNF inhibitors with regard to psoriatic skin involvement[8] and dactylitis. TNF inhibitors, including certolizumab pegol, have also been shown to slow the progression of joint damage. Following advances in the understanding of the pathogenesis of PsA and the need to consider effective treatments that improve all disease manifestations, several treatment guidelines have been published, and subsequently updated, highlighting the important aspects to be considered when initiating a biologic or non-biologic treatments, including in patients who have failed only one cDMARD. For example:	

- BSR treatment guidelines recommend considering TNF inhibitors for a subset of patients who have failed only one DMARD where there is evidence of adverse prognostic factors;
- The international GRAPPA guideline (which also accounts for the disease severity) and the EULAR recommendations currently guide treatment of PsA and both clearly emphasize in their overarching principles the need to account for the extra articular manifestations (e.g. those with predominant axial disease, predominant nail involvement, dactylitis and/or predominant enthesitis) when managing patients with PsA.

Table 1: Summary of latest BSR, GRAPPA and EULAR treatment recommendations for PsA

Guideline	Recommendation	Further details
British Society for Rheumatology (BSR)[10]	Peripheral arthritis, (i) TNF inhibitor therapy may be considered for patients who have failed only one cDMARD where there is evidence of certain adverse prognostic factors	The guideline specifically state that these prognostic factors are: '*five or more swollen joints in association with elevated C-reactive protein persisting for >3 months or structural joint damage due to disease'*
EULAR[8]	Recommendation 5: *'In patients with peripheral arthritis and an inadequate response to at least one cDMARD, therapy with a biological DMARD, usually a TNF inhibitor, should be commenced.*' Recommendation 8: *'In patients with active enthesitis and/or dactylitis and insufficient response to NSAIDs or local glucocorticoid injections, therapy with a biological DMARD should be considered, which according to current practice is a TNF inhibitor.'*	The recommendations also state: *'In patients with peripheral arthritis in whom a csDMARD (usually MTX because of its effects on joints and skin, but also leflunomide, sulfasalazine or others, see above) is not efficacious (ie, the treatment target of at least low disease activity has not been reached) even though the treatment has been taken for an appropriate length of time (usually 3–6 months), a bDMARD can be considered'* *'after failure of local or non-specific anti-inflammatory therapy, biological DMARDs may be applied even if no cDMARDs have been tried, since the latter have not been proven efficacious in treating these aspects of PsA, especially enthesitis'*

	Recommendation 9: *'In patients with predominantly axial disease that is active and has insufficient response to NSAIDs, therapy with a biological DMARD should be considered, which according to current practice is a TNF inhibitor.'*	*'This recommendation applies to the subgroup of patients with PsA who have predominant and active axial disease. Active disease here is usually defined in reference to a Bath Ankylosing Spondylitis Disease Activity Index above 4 points. In these patients, bDMARDs can be considered even if no csDMARDs have been tried, since csDMARDs have no proven efficacy in axial disease.'*
GRAPPA[4]	TNF inhibitors are strongly recommended for: • Peripheral arthritis, inadequate response to DMARDs • Axial PsA • Enthesitis • Dactylitis • Nail psoriasis	cDMARDs are specifically not recommended by GRAPPA in such cases of predominant extra articular manifestations.

UCB thus considers that given the heterogeneous nature of PsA and the need to effectively manage all its clinical manifestations, it is important for NICE to allow use of certolizumab pegol in a certain type of patients in cases where a second cDMARD would be ineffective and not recommended as per the above treatment guidelines. We believe that the importance of managing all the disease manifestations has also been noted in the patient and clinician submissions to the committee, and should thus be accounted for.

Furthermore, as per the UCB submitted evidence, data from the RAPID-PsA study showed that, in the subgroup of patients who are TNF inhibitor naïve and have only received one prior cDMARD (i.e. subpopulation 1), certolizumab pegol has demonstrated rapid and sustained improvements in signs and symptoms, in terms of both the joint and skin manifestations of the disease, greater improvements in physical functioning, extra-articular manifestations of disease, including nail involvement, enthesitis, dactylitis and axial involvement, as well as improvements in a broad spectrum of patient relevant outcomes (e.g. pain, fatigue, HRQoL, workplace and household productivity).

	Based on the above considerations, and given the recommendations from the BSR for use of TNF inhibitors in certain types of patients with an inadequate response to only one cDMARD, together with similar recommendations from both EULAR and GRAPPA, we consider that there is a clear and consistent mandate stated in the latest clinical practice guidelines to use a TNF inhibitor in certain types of patients who have had an inadequate response to only one cDMARD and where a second cDMARD might not be an effective treatment option. Recommendation of certolizumab pegol in certain types of patients with an inadequate response to only one cDMARD as per the EULAR and GRAPPA guidelines, would bring the NICE guidance in line with clinical practice guidelines in both the UK and Europe. This would therefore broaden the therapeutic armamentarium, with an effective treatment option for patients and clinicians, in a heterogeneous condition where it is important to manage a wide range of manifestations. UCB thus requests that the Appraisal Committee reviews and considers the decision to withhold the recommendation of certolizumab pegol in subpopulation 1.	
UCB	**Response to topics of interest highlighted by the Appraisal Committee** • <u>Has all of the relevant evidence been taken into account?</u> UCB has no further comment on this point.	Comment noted
UCB	• <u>Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?</u> 1. Adjustment of the placebo creep in the UCB submitted NMA The ACD states in section 4.6, page 9 and in the Summary table on page 29 that '*The committee concluded that because these issues had either not been accounted for (secukinumab) or because it was unclear how they had been accounted for (certolizumab pegol) in the company submissions, it was not possible to make reliable conclusions about the difference in the efficacy of certolizumab pegol and secukinumab using the companies' analyses*'. UCB would like to reiterate that this statement does not accurately reflect the evidence submitted. The occurrence of placebo creep and class effect were in fact accounted for in the analysis submitted by UCB; i.e. the adjusted meta-regression mixed treatment comparison for ACR 20/50, PASI75 and PsARC accounted for an association between the results for absolute effect in placebo arms across PsA studies identified by systematic literature review. Additionally, section 4.10 of the UCB submission states that: '*Due to the substantial level of heterogeneity on baseline risk, the results of meta-regression in TNF inhibitor naïve subpopulation presented here are based on treating [*TNF inhibitors] *as sharing a class effect (but with the possibility of variation within that class), along with controlling for baseline risk (i.e., variation in placebo response). The other biologic treatments (e.g.*	1. Thank you for your comment. The Assessment Group noted that the adjustment for placebo creep had been made however there were no sufficient information for them to reproduce the analysis and therefore they could not critique it. No change has been made in the FAD.

	[secukinumab]*) also had its odds-ratios controlled for baseline risk, but it essentially belonged to its own 'class', and thus did not 'borrow strength' from each other or any other drug.* ' The approach considered by UCB was subsequently acknowledged by the AG in their report. For example, table 131 on page 325 of the AG report summarises the key assumptions in the synthesis models for PsARC responses and states that the UCB model was '*adjusted for* [placebo response in] *the biologic naïve subpopulation*'. Furthermore, the adjusted NMA accounting for the placebo creep and class effect were used as inputs in the UCB cost-effectiveness model, which was similar to the AG approach. UCB thus requests that the statement in the ACD is revised to accurately reflect the UCB submitted 2. Summary of evidence for improvement of joint symptoms In section 4.11 of the ACD (page 13) is stated that '*The committee concluded that although there were limitations in the analyses, it considered that certolizumab pegol and secukinumab were similar to the other therapies in improving joint symptoms in both biological-naive and experienced subpopulations*'. UCB considers that use of the broad term 'other therapies' is not reflecting the committee meeting discussions and the clinical feedback summarized in Section 4.11, which was referring to TNF alpha inhibitors. We request that the text be amended to (revision underlined): '*The committee concluded that although there were limitations in the analyses, it considered that certolizumab pegol and secukinumab were similar to <u>TNF alpha inhibitors</u> in improving joint symptoms in both biological-naive and experienced subpopulations*'. 3. Summary of safety profiles In Section 4.12, page 13 of the ACD, it has been stated that: '…..*there was no concern about additional adverse events for certolizumab pegol and secukinumab over other biological therapies. The committee concluded that the safety profiles of certolizumab pegol and secukinumab were comparable*'. UCB requests that the statement be revised to correctly specify the appropriate comparison being referred to, as per the committee meeting discussions (suggested revision underlined): '*there was no concern about additional adverse events for certolizumab pegol and secukinumab over other <u>TNF inhibitors</u>. The committee concluded that the safety profiles of certolizumab pegol and secukinumab were comparable <u>to the other TNF inhibitors'</u>*.	2. Thank you for your comment. The FAD has been revised. 3. Thank you for your comment. The FAD has been revised.

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Are the recommendations sound and a suitable basis for guidance to the NHS?

Section 4.2, page 8 of the ACD indicates that 'The committee heard from the clinical experts that both certolizumab pegol and secukinumab 300mg were effective therapies and that secukinumab was particularly effective in severe psoriasis.' UCB considers that this summary of the clinical experts' opinion is unclear given that the focus of the guidance should be on the joints rather than skin. Therefore, UCB requests that the text be revised to indicate (revision underlined): '…that secukinumab 300mg was particularly effective in treating symptoms of psoriasis in PsA patients with severe psoriasis.'
Section 4.10, page 12 of the ACD states 'The clinical experts agreed that patients with early primary treatment failure would respond differently to a subsequent second biological therapy (that is, TNF-alpha inhibitors).' UCB considers that this statement does not accurately reflect the clinical expert input during the first Appraisal Committee meeting and requests that the statement be revised to (text underlined): 'The clinical experts agreed that patients with primary treatment failure would respond differently to a subsequent second biological therapy (that is, TNF-alpha inhibitors) than patients who had not previously experienced primary failure.'

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<td>Thank you for your comment. The committee heard that the clinical experts were referring to secukinumab as being effective for psoriasis as per the NICE TA350 guidance.

Thank you for your comment. The section 4.10 of the FAD has been revised.</td>
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Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?
UCB has no comment on this point.

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<td>Comment noted</td>
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Factual inaccuracies
A summary of the factual inaccuracies included in the document is provided in Table 2.

Table 2: Summary of factual inaccuracies in the ACD
<table>
<tr><th>Page</th><th>Content from the ACD report</th><th>UCB comment</th></tr>
<tr><td>3</td><td>Paragraph 1.1 of the ACD states:
'Certolizumab pegol is only recommended if the company provides it agreed in the patient access scheme.'</td><td>Revision underlined:
'Certolizumab pegol is only recommended if the company provides it as agreed in the approved patient access scheme'</td></tr>
<tr><td>3</td><td>Paragraph 1.2 of the ACD states:
'Secukinumab alone, or in combination with methotrexate, is recommended as an option for treating active psoriatic arthritis in adults only if:</td><td>This recommendation is incomplete as it omits the fact that secukinumab is only licensed for use in patients who have already received biologic therapies at a dose of 300mg (see</td></tr>
</table>
</td>
<td>Thank you for your comment. Most factual inaccuracies have been addressed in the FAD.

The recommended dosing are detailed in section</td>
</tr>
</table>

		• *it is used as described in the NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis (recommendations 1.1 and 1.2) or* • *the person has had a TNF-alpha inhibitor but their disease has not responded within the first 12 weeks or has stopped responding after 12 weeks or* • *TNF-alpha inhibitors are contraindicated but would otherwise be considered (as described in NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis).*'	section 4.18 of the ACD). UCB therefore requests that NICE amend the wording in line with the approved posology of secukinumab. The text should be amended to (revision underlined): '*Secukinumab alone, or in combination with methotrexate, is recommended as an option for treating active psoriatic arthritis in adults only if:* • *it is used as described in the NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis (recommendations 1.1 and 1.2) or* • *<u>[at the 300mg dose]</u> the person has had a TNF-alpha inhibitor but their disease has not responded within the first 12 weeks or has stopped responding after 12 weeks or* • *TNF-alpha inhibitors are contraindicated but would otherwise be considered (as described in NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis).*'	4.18. No change has been made in the FAD.
	6	In Section 2 of the ACD (Price) it is stated: '*The company has agreed a patient access scheme with the Department of Health. The first 12 weeks of therapy with certolizumab pegol will be free of charge.*'	This statement is incomplete and the following text should be added (revision underlined): '*The company has agreed a patient access scheme with the Department of Health. The first 12 weeks of therapy with certolizumab pegol will be free of charge. <u>The Department of Health considered that this patient access scheme does not constitute an excessive administrative burden on the NHS</u>*'	Comments noted. The FAD has been revised.

	17 and 22	In Section 4.18 and in the summary table of the ACs key conclusions, subpopulation 3 is referred to as: '*Subpopulation 3: patients who have had biological therapies*'	The subpopulation definition should be amended to (revision underlined): '*Subpopulation 3: patients who have had TNF-alpha inhibitors'*	Comments noted. The FAD has been revised.
	23	The summary table of the ACs key conclusions contains the following: '*People with psoriatic arthritis whose disease has not responded adequately to 2 DMARDs and whose disease has not responded adequately to DMARDs*'	The statement contains a duplication and should be revised to: '*People with psoriatic arthritis whose disease has not responded adequately to 2 DMARDs*'	Comments noted. The FAD has been revised.
	32-33	The ACD states that: '*The committee concluded that certolizumab pegol is cost effective in 2 subpopulations….with ICERs below, or close to, £20,000 per QALY gained when taking into account the proposed patient access scheme for certolizumab pegol'*	Given that the PAS for certolizumab has been agreed with the Department of Health, we would request the text to be amended as follows (revision underlined): '*The committee concluded that certolizumab pegol is cost effective in 2 subpopulations….with ICERs below, or close to, £20,000 per QALY gained when taking into account the approved patient access scheme for certolizumab pegol'*	Comments noted. Section 2 of the FAD states that the patient access scheme has been approved. No change has been made in the FAD.
	35	In Section 5.4 of the ACD the approved PAS for certolizumab pegol is summarised as: '…..*The Department of Health and UCB have agreed that a patient access scheme for certolizumab pegol which provides a rebate to the list price of certolizumab pegol, applied at the point of purchase or invoice. The NHS will not pay for certolizumab pegol for the first 12 weeks. The size of these discounts is commercial in confidence. It is the responsibility of the companies to communicate details of the discount to the relevant NHS organisations*.'	The text inaccurately implies that the certolizumab pegol PAS is a discount and that it is commercial in confidence. We would thus request the following revisions (text underlined) to ensure clarity in the description of the PAS: '*The Department of Health and Novartis have agreed that secukinumab will be available to the NHS with a patient access scheme which makes it available with a discount. The size of the discount is commercial in confidence. The Department of Health and UCB Pharma have agreed that certolizumab pegol will be available to the NHS with a patient access scheme. UCB Pharma will provide the first 12 weeks of certolizumab pegol free of charge, which is equivalent to 10 vials. It is the responsibility of*	Comments noted. The FAD has been revised. .

			the companies to communicate details of the discount/patient access scheme to the relevant NHS organisations.'	
Novartis	Novartis firmly believes that secukinumab represents both a clinically- and cost-effective treatment option for subpopulation 1. The Novartis submission demonstrated secukinumab to be cost-effective versus best supportive care (represented by the placebo arm of the one prior DMARD population in FUTURE 2, in which 79% of patients were receiving methotrexate) in this subpopulation 1. The robustness of this result was confirmed in analyses provided in response to the initial appraisal consultation document (utilising 12 week, rather than 16 week data for secukinumab, aligned to the Assessment Group's model). Furthermore, since the Assessment Group considered it appropriate to use the entire biologic naïve population data to generate effect estimates for the 1 DMARD analyses, cost-effectiveness of secukinumab versus the biologic therapies in subpopulation 1 can be inferred from the subpopulation 2 analyses. Subpopulation 2 analyses in both the Novartis submission and the Assessment Group report support the cost-effectiveness of secukinumab versus other biologic therapies. However, we have taken the decision not to provide further evidence or reiterate detailed argumentation in relation to subpopulation 1 within our response to the second appraisal consultation document (ACD2). We have therefore limited our response to three matters of factual inaccuracy and three suggested wording changes to remove duplication and improve clarity.			Thank you for your comment. The Committee considered all the evidence submitted, including evidence from clinical trials, patient and clinical experts, the Assessment Group's economic analysis and the companies' submissions. It also carefully considered the comments received from C&Cs in response to the Assessment Report. The committee concluded that certolizumab pegol and secukinumab could not be recommended as treatment options for people with psoriatic arthritis whose disease had not responded adequately to 1 DMARD, as specified in section 4.16 of the final appraisal determination (FAD)
Novartis	**Factual inaccuracies** 1. Inaccurate reference to the EULAR guidelines This inaccuracy was mentioned in our response to the initial ACD (see pages 2 & 4).			Thank you for your comment. The reference to EULAR has been

	The statement, on pages 7 and 24 of ACD2, that "people usually have 2 DMARDs before progressing to biological therapies (in line with guidelines from the British Society for Rheumatology [BSR] and the European League Against Rheumatism [EULAR], and in line with NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis)" is factually inaccurate because the EULAR guideline[1] clearly recommends use of biologic therapy following 1 DMARD. It states: "In patients with peripheral arthritis and an inadequate response to ***at least one csDMARD***, therapy with a bDMARD, usually a TNF inhibitor, should be commenced" [emphasis added; csDMARD = conventional DMARD, bDMARD = biologic DMARD)]. The statement that use of 2 DMARDs prior to biological therapy is 'in line with' this guideline is therefore factually inaccurate. **Requested Action: Omit reference to EULAR guidelines** Please amend the sentence on pages 7 and 24 to read: "people usually have 2 DMARDs before progressing to biological therapies (in line with guidelines from the British Society for Rheumatology [BSR], and NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis)". 2. <u>Clarification regarding other therapies offering similar efficacy</u> On pages 13 and 29 the statement that the committee "considered that certolizumab pegol and secukinumab were similar to the other therapies in improving joint symptoms in both biological-naive and experienced subpopulations" is misleading, since "other therapies" could be interpreted to include apremilast. It is clear that the committee concluded that "Both certolizumab pegol and secukinumab were consistently more effective than apremilast" (see page 12 of ACD2). **Requested Action: Clarify that secukinumab is similar to other *biological* therapies** Please amend the sentence on pages 13 and 29 to read: "considered that certolizumab pegol and secukinumab were similar to the other ***biological*** therapies in improving joint symptoms in both biological-naive and experienced subpopulations". 3. <u>Incomplete description of secukinumab's mechanism of action</u> On page 4, a greater level of detail is provided on certolizumab pegol's mechanism of action in comparison to that provided for secukinumab. **Requested Action: Add the following detail to the description of secukinumab** On page 4 please amend the text on the description of secukinumab to read: "Secukinumab (Cosentyx, Novartis) is a fully human monoclonal antibody that selectively neutralises interleukin 17A (IL-17A)".	removed in section 4.2 of the FAD. Thank you for your comment. Factual inaccuracies 2 and 3 have been addressed in the FAD.
Novartis	**Suggested wording changes to remove duplication and aid clarity**	Thank you for your comment. The wording

	We would like to highlight two areas of apparent duplication within the summary of the appraisal committee's key conclusions, and suggest inclusion of specific drug names within the summary of the technologies to improve clarity. a) On page 21 and on page 30-31, we query whether both the below sentences are necessary, and propose that the first sentence may be more appropriate in the summary section, since the second sentence is found on page 16: • "The committee added that given the potential shift in clinical practice for psoriatic arthritis, it needed to be very certain about the cost effectiveness of certolizumab pegol and secukinumab in subpopulation 1." • "The committee added that given this potential shift in use of biological therapy for psoriatic arthritis, and in particular for new technologies, one of which has a different mechanism of action (see section 4.2), it needed to be very certain about the cost effectiveness of certolizumab pegol and secukinumab in subpopulation 1." b) On page 23, we query whether both the below phrases are necessary: • "whose disease has not responded adequately to 2 DMARDs and" • "whose disease has not responded adequately to DMARDs and" c) On page 25 we suggest that the drug names be added to clarify which patient populations are considered appropriate for each specific treatment., i.e.; • "***Secukinumab is for*** patients with psoriatic arthritis whose disease has not responded adequately to at least 2 DMARDs and TNF-alpha inhibitors within the first 12 weeks or has stopped responding after 12 weeks" • "***Certolizumab pegol is for*** patients with psoriatic arthritis whose disease has not responded to at least 2 DMARDs and has stopped responding to TNF-alpha inhibitor after the first 12 weeks" • "***Secukinumab is for*** patients in whom TNF-alpha inhibitors are contraindicated".	has been revised in the FAD.

Comments received from commentators

Commentators	Comment [sic]	Response
Abbvie	Section 1.3, page 3 of the ACD2 contains the statement "Assess the response to certolizumab pegol and secukinumab after 12 weeks and 16" AbbVie is particularly concerned that this statement is going to introduce an unwarranted level of complexity in clinical practice, with the risk that some patients may unnecessarily be delayed in their subsequent disease assessment if two thresholds (of 12 and 16 weeks) are recommended.	Thank you for your comment. The committee noted that the times of responses assessment described in the FAD are in line with the 'Summary of Product Characteristics' of certolizumab pegol and secukinumab. No change has been made to the FAD
Abbvie	Section 4.1 of the ACD2, page 7 AbbVie believes that the following sentence: "The committee heard from the clinical experts that psoriatic arthritis not only affects joints and tendons but can also be associated with other debilitating conditions of the skin, bowel and eye and with metabolic syndrome." should be followed by: "The Committee recognizes that secukinumab has not demonstrated clinical effectiveness in inflammatory bowel disease".	Thank you for your comment. The committee concluded that because these issues had not been discussed during the appraisal meeting, there should be no change to the FAD.
Abbvie	Section 4.2 of the ACD2, page 8 AbbVie believes that the sentence "The clinical experts commented that certolizumab pegol targets TNF-alpha and that secukinumab has a different mechanism of action, targeting interleukin 17A (IL-17A), which could potentially benefit people in whom TNF-alpha inhibitors are contraindicated or not tolerated" should be followed by a statement clarifying that TNF-alpha are the preferred first-line biologic agents.	Comment noted

Commentators	Comment [sic]	Response
Abbvie	Section 4.11 of the ACD2, pages 12-13 Abbvie wishes to highlight that psoriatic arthritis is a multi-faceted disease composed of arthritis, psoriasis and extra-articular manifestations/ comorbidities such as Inflammatory bowel disease. The Appraisal Committee should take into consideration the study by Hueber et al (2012), and, after the sentence: "The clinical experts stated that they could not distinguish between the TNF-alpha inhibitors in improving joint symptoms in clinical practice and would therefore choose 1 of the therapies based on availability and the patient's comorbidities", it should include the statement "Secukinumab has failed to demonstrate clinical effectiveness in the extra-articular component of psoriatic arthritis, as demonstrated in patients with Crohn's disease".	Thank you for your comment. The committee concluded that because these issues had not been discussed during the appraisal meeting, there should be no change to the FAD.

Celgene	**Celgene agrees with the Committee's decision not to recommend CZP and SEC in sub population 1 (biologic-naïve patients who have received one prior DMARD)** According to NICE guidance (TA199,[1] TA220[2]), the NICE commissioning algorithm for biologic drugs for the treatment of psoriatic arthritis,[3] and the British Society for Rheumatology 2012 guidelines,[4] the biologic agents adalimumab, etanercept, infliximab and golimumab are recommended in patients who have not responded to adequate trials of at least **two** standard DMARDs, administered either individually or in combination. Accordingly, if the cost-effectiveness of CZP and SEC is to be considered in subpopulation 1, Celgene considers that the appropriate comparator, i.e. a **second non-biologic DMARD (and not Best Supportive Care)**, should be used to reflect routine NHS practice. This would also be consistent with the Final Scope for this appraisal which lists the following comparators: *For people who have only received 1 prior non-biological disease modifying anti-rheumatic drug (DMARD)* • *Disease modifying anti-rheumatic drugs* *For people whose disease has not responded adequately to at least 2 DMARDs:* • *Biological therapies (with or without methotrexate including etanercept, adalimumab, infliximab, golimumab, apremilast [subject to ongoing NICE appraisal]),* *For people whose disease has not responded adequately to DMARDs and not adequately responded to biological therapies (including etanercept, adalimumab, infliximab and golimumab) or biological therapies are contraindicated:* • *Ustekinumab* • *Apremilast [subject to ongoing NICE appraisal]* • *Best supportive care.* Additionally, Celgene notes that the marketing authorization for CZP and SEC is aligned to that of other biologics licensed for psoriatic arthritis and considers that a similar approach to evaluating their use on the NHS should be taken to ensure consistency with previous NICE appraisals (TA199, TA220). Celgene notes that the York AG makes similar reference when discussing limitations of their analyses (Assessment Report p.248-9): *"…subpopulation 1 only includes the comparators CZP, SEC and BSC, as per the NICE scope. It is recognised however, that there may be other comparators relevant for this subpopulation. In particular, patients who have only received 1 prior DMARD may be eligible to receive a 2nd DMARD. It was not possible within the scope of this appraisal to assess the evidence for DMARDs and therefore include this as*	Comment noted

Commentators	Comment [sic]	Response
	a formal comparator in this subpopulation. The extremely low cost of DMARDs (7.5 mg of MTX is £0.30) make it likely that these would be considered cost-effective in this population…" Celgene notes that the AG have stated that BSC is listed as a comparator for sub population 1 however this is <u>not</u> consistent with the final scope for this appraisal for which BSC is only included as a comparator for people whose disease has not responded adequately to DMARDs and not adequately responded to biological therapies (including etanercept, adalimumab, infliximab and golimumab) or biological therapies are contraindicated. In the first ACD, the Committee noted: *"For subpopulation 1 (1 previous DMARD but no biological therapy), the committee noted that the comparators in the assessment group's model and the group represented by the biological-naive subpopulation did not reflect clinical practice in England. For these reasons, the committee concluded that certolizumab pegol and secukinumab could not be recommended as treatment options for people with psoriatic arthritis whose disease had not responded adequately to 1 DMARD."* Celgene agrees with the provisional recommendations made in the ACD not to recommend CZP and SEC in patients that are biologic-naïve who have received one prior DMARD. The manufacturers have not submitted analyses comparing against the relevant comparator in routine NHS practice, a second non-biologic DMARD, and it is highly unlikely that either of these technologies would be considered cost-effective at this stage in the pathway based on the comments made by the York AG. Celgene considers that, should the Committee wish to evaluate SEC and CZP in sub population 1, this should take place alongside a review of existing NICE Guidance for recommended technologies for PsA to ensure a consistent approach.	

Celgene	**Comments on the additional analysis submitted by Novartis in sub population 1** During consultation, Novartis have submitted an additional cost-effectiveness analysis for sub population 1. Celgene considers this analysis to be flawed for a number of reasons, with a high degree of uncertainty and should therefore be interpreted with extreme caution. Whilst the additional clinical data used for SEC from FUTURE 2 appears to be more relevant to sub population 1, the comparator efficacy data used in this analysis is not appropriate, for the following reasons: 1. The NICE final scope for this appraisal states that a second DMARD and **not** BSC is the appropriate comparator in this population (see above). 2. FUTURE 2 is not an active comparator study and compares SEC versus placebo. The placebo arm of the SEC FUTURE 2 trial is likely to underestimate the efficacy of the appropriate comparator in this position and favour SEC in the analysis. 3. No attempt to assess the clinical evidence for DMARDs in this sub population has been made by the manufacturer (or the AG) resulting in a high degree of uncertainty. In the second ACD, the Committee comment (section 4.16): *"The committee heard from the assessment group that the analysis done by Novartis only included secukinumab and best supportive care and therefore was lacking the full comparator set for subpopulation 1, in particular the other biological treatments (etanercept, infliximab, adalimumab and golimumab), which according to their licences could be used in subpopulation 1."* Celgene agrees with the Committee comments that the full range of comparators may not have been included for sub population 1, but does not agree that the important omission relates primarily to TNF-alpha inhibitors. Based on expert opinion, TNF-alpha inhibitors are not routinely used after 1 DMARD in NHS practice as existing NICE Guidance (TA199 and TA220) restricts reimbursement to after 2 or more DMARDs. Celgene considers that the most important omission in the Novartis analysis relates to the exclusion of a second DMARD as a formal comparator in this sub population. Until the manufacturer is able to assess the clinical evidence for the use of a DMARD in this sub population through a systematic literature review, and present the cost-effectiveness results in a fully incremental analysis relative to the full comparator set, there remains a high degree of uncertainty with the company conclusions. It would not be sufficient to simply include the TNF-alpha inhibitors as comparators in this sub population as this would still lack the second DMARD, which is most relevant to routine NHS practice. As stated previously, modelling BSC and using the PBO arm from the SEC trials to inform the efficacy introduces a significant amount of uncertainty and is not considered appropriate for this comparison.	Comment noted

Commentators	Comment [sic]	Response
	Celgene also notes that the current recommendations for SEC made by the Scottish Medicines Consortium (SMC) in July 2016 are restricted and do not include sub population 1.[i] In summary, neither manufacturer have presented sufficiently robust cost-effectiveness evidence versus a second DMARD to justify a recommendation in sub population 1 and Celgene agrees fully with the Committee's provisional "not recommended" in this population.	
Psoriasis Association	Psoriatic arthritis can affect people of any age, and often it affects people in young or 'mid' adulthood who should, otherwise, be 'in their prime', pursuing careers, relationships and families. Crucially, without timely and effective treatment, the damage – and associated symptoms and impacts – caused by psoriatic arthritis can be permanent. Both of these treatments work to modify the disease itself, and also work in a different manner to the currently-available anti-TNFs, meaning they are both useful options for people who may not have experienced adequate results with anti-TNFs, or cannot take them.	Comment noted

The following consultees/commentators indicated that they had no comments on the appraisal consultation document:

British Association of Dermatologists
Department of Health
Merck Sharp & Dohme
The Psoriasis and Psoriatic Arthritis Association

[i] https://www.scottishmedicines.org.uk/files/advice/secukinumab_Cosentyx__sA_FINAL_July_2016_for_website.pdf (accessed Jan 2017)

Novartis Pharmaceuticals UK Ltd
Frimley Business Park
Frimley
Camberley
Surrey GU16 7SR

Mr M Boysen
Programme Director, Centre for Health Technology Evaluation
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M1 4BT

27th January 2017

Dear Mr Boysen,

Re: Novartis response to the second Appraisal Consultation Document for ID579

Thank you for the opportunity to comment on the second Appraisal Consultation Document (ACD) for this appraisal. We continue to welcome the committee's recommendation of secukinumab for subpopulations 2–4 i.e. patients who have had at least 2 previous DMARDs and no biological therapy, patients who have had biological therapies and patients who in whom TNF-alpha inhibitors are contraindicated. However, we are frustrated and disappointed by NICE's decision to issue a second ACD, despite no major change to the recommendation for subpopulation 1 (1 previous DMARD but no biological therapy) versus the initial ACD.

Novartis firmly believes that secukinumab represents both a clinically- and cost-effective treatment option for subpopulation 1. The Novartis submission demonstrated secukinumab to be cost-effective versus best supportive care (represented by the placebo arm of the one prior DMARD population in FUTURE 2, in which 79% of patients were receiving methotrexate) in this subpopulation 1. The robustness of this result was confirmed in analyses provided in response to the initial appraisal consultation document (utilising 12 week, rather than 16 week data for secukinumab, aligned to the Assessment Group's model). Furthermore, since the Assessment Group considered it appropriate to use the entire biologic naïve population data to generate effect estimates for the 1 DMARD analyses, cost-effectiveness of secukinumab versus the biologic therapies in subpopulation 1 can be inferred from the subpopulation 2 analyses. Subpopulation 2 analyses in both the Novartis submission and the Assessment Group report support the cost-effectiveness of secukinumab versus other biologic therapies.

However, we have taken the decision not to provide further evidence or reiterate detailed argumentation in relation to subpopulation 1 within our response to the second appraisal consultation document (ACD2). We have therefore limited our response to three matters of factual inaccuracy and three suggested wording changes to remove duplication and improve clarity.

Factual inaccuracies

1. Inaccurate reference to the EULAR guidelines

This inaccuracy was mentioned in our response to the initial ACD (see pages 2 & 4).

The statement, on pages 7 and 24 of ACD2, that "people usually have 2 DMARDs before progressing to biological therapies (in line with guidelines from the British Society for Rheumatology [BSR] and the European League Against Rheumatism [EULAR], and in line with NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis)" is factually inaccurate because the EULAR guideline[1] clearly recommends use of biologic therapy following 1 DMARD. It states: "In patients with peripheral arthritis and an inadequate response to ***at least one csDMARD***, therapy with a bDMARD, usually a TNF inhibitor, should be commenced" [emphasis added; csDMARD = conventional DMARD, bDMARD = biologic DMARD)]. The statement that use of 2 DMARDs prior to biological therapy is 'in line with' this guideline is therefore factually inaccurate.

Requested Action: Omit reference to EULAR guidelines

Please amend the sentence on pages 7 and 24 to read: "people usually have 2 DMARDs before progressing to biological therapies (in line with guidelines from the British Society for Rheumatology [BSR], and NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis)".

2. Clarification regarding other therapies offering similar efficacy

On pages 13 and 29 the statement that the committee "considered that certolizumab pegol and secukinumab were similar to the other therapies in improving joint symptoms in both biological-naive and experienced subpopulations" is misleading, since "other therapies" could be interpreted to include apremilast. It is clear that the committee concluded that "Both certolizumab pegol and secukinumab were consistently more effective than apremilast" (see page 12 of ACD2).

Requested Action: Clarify that secukinumab is similar to other *biological* therapies
Please amend the sentence on pages 13 and 29 to read: "considered that certolizumab pegol and secukinumab were similar to the other ***biological*** therapies in improving joint symptoms in both biological-naive and experienced subpopulations".

3. Incomplete description of secukinumab's mechanism of action

On page 4, a greater level of detail is provided on certolizumab pegol's mechanism of action in comparison to that provided for secukinumab.

Requested Action: Add the following detail to the description of secukinumab
On page 4 please amend the text on the description of secukinumab to read: "Secukinumab (Cosentyx, Novartis) is a fully human monoclonal antibody that selectively neutralises interleukin 17A (IL-17A)".

Suggested wording changes to remove duplication and aid clarity

We would like to highlight two areas of apparent duplication within the summary of the appraisal committee's key conclusions, and suggest inclusion of specific drug names within the summary of the technologies to improve clarity.

a) On page 21 and on page 30-31, we query whether both the below sentences are necessary, and propose that the first sentence may be more appropriate in the summary section, since the second sentence is found on page 16:

- "The committee added that given the potential shift in clinical practice for psoriatic arthritis, it needed to be very certain about the cost effectiveness of certolizumab pegol and secukinumab in subpopulation 1."
- "The committee added that given this potential shift in use of biological therapy for psoriatic arthritis, and in particular for new technologies, one of which has a different mechanism of action (see section 4.2), it needed to be very certain about the cost effectiveness of certolizumab pegol and secukinumab in subpopulation 1."

b) On page 23, we query whether both the below phrases are necessary:

- "whose disease has not responded adequately to 2 DMARDs and"
- "whose disease has not responded adequately to DMARDs and"

c) On page 25 we suggest that the drug names be added to clarify which patient populations are considered appropriate for each specific treatment., i.e.;

- "***Secukinumab is for*** patients with psoriatic arthritis whose disease has not responded adequately to at least 2 DMARDs and TNF-alpha inhibitors within the first 12 weeks or has stopped responding after 12 weeks"
- "***Certolizumab pegol is for*** patients with psoriatic arthritis whose disease has not responded to at least 2 DMARDs and has stopped responding to TNF-alpha inhibitor after the first 12 weeks"
- "***Secukinumab is for*** patients in whom TNF-alpha inhibitors are contraindicated".

Concluding remarks

Novartis requests that this appraisal now be brought to the swiftest possible conclusion and we look forward to the committee meeting on 28th February 2017. By TAG implementation, eligible UK patients with psoriatic arthritis will already have been denied access to this innovative therapy for *at least* 21 months post EMA marketing approval (EMA approval was granted in November 2015, earliest estimated TAG implementation date is August 2017), and therefore we request that final guidance publication (TAG) is expedited soon after the committee meeting and no later than end May 2017.

Yours sincerely,

[redacted]

References

1. Gossec L, Smolen JS, Ramiro S, de Wit M, Cutolo M, Dougados M, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. *Ann Rheum Dis* 2016;75:499-510.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXELLENCE

Multiple Technology Appraisal (MTA)

Certolizumab pegol (Cimzia®) for treating active psoriatic arthritis following inadequate response to disease modifying anti-rheumatic drugs
[ID579]

27 January 2017

UCB response to the second Appraisal Consultation Document

Introduction

UCB welcomes the opportunity to respond to the second Appraisal Consultation Document (ACD).

We are pleased with the preliminary decision to recommend certolizumab pegol as a treatment option for treating active psoriatic arthritis (PsA) following inadequate response to disease modifying antirheumatic drugs (DMARDs) and appreciate that many of our comments on the first ACD have been taken into consideration.

Following a review of the second ACD, UCB would like to provide a number of comments and observations for consideration, which UCB believes will have significance for the discussions at the next Appraisal Committee meeting. A summary of the key points raised is outlined below and detailed further in the next sections.

Outline of Responses

Section 1: General comments

UCB understands that the Committee has concluded that both certolizumab pegol and secukinumab could not be recommended as treatment options for subpopulation 1 (patients who are TNF inhibitor naïve and had only one prior cDMARD). UCB would like to reiterate that as per the most recent UK-based and international clinical practice guidelines, EULAR and GRAPPA, TNF inhibitors could be used in certain types of patients with an inadequate response to only one cDMARD (eg characterized by the presence of axial or extra-articular manifestations of disease). UCB thus considers that given the heterogeneous nature of PsA and the need to effectively manage all its clinical manifestations, it is important for NICE to allow use of certolizumab pegol in a certain type of patients in cases where a second cDMARD would be ineffective and is not recommended as per the clinical practice treatment guidelines.

Section 2: Response to topics of interest highlighted by the Appraisal Committee

- Topic 1: Has all of the relevant evidence been taken into account?
- Topic 2: Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Topic 3: Are the recommendations sound and a suitable basis for guidance to the NHS?
- Topic 4: Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?

Section 3: Factual inaccuracies

1 General comments

1.1 Reconsideration of recommendations for certolizumab pegol in Subpopulation 1 (biologic naïve with one prior cDMARD) in their guidance to the NHS

Section 4.2, page 7 of the ACD states that: '*The committee heard from the clinical and patient experts that the psoriatic arthritis population is heterogeneous. Some people's disease responds to the first disease-modifying anti-rheumatic drug (DMARD), whereas some people's disease may respond to a second or a third DMARD. Some people's disease may not respond all.… The committee was aware that the British Society for Rheumatology guidelines also mention that biological therapies (that is, tumour necrosis factor [TNF]-alpha inhibitors) can be considered in people with specific prognostic factors (including 5 or more swollen joints together with elevated C-reactive protein persisting for more than 3 months or structural joint damage caused by disease) when 1 DMARD has not worked*'.

Furthermore, in section 4.16, pages 15-16 of the ACD it is stated that: '...*However, the committee was not convinced that the use of biological therapy after 1 DMARD is established clinical practice in the NHS (see section 4.2) and if it is, in which specific group of people it is used….. The committee concluded it was unable to recommend certolizumab pegol and secukinumab as treatment options for people with psoriatic arthritis whose disease had not responded adequately to 1 DMARD*'.

UCB understands how the Appraisal Committee reached this conclusion and that it was unable to recommend certolizumab pegol in subpopulation 1 (i.e. biologic naïve patients who have not responded adequately to only one cDMARD). However UCB would like to reiterate that:

1. the GRAPPA and EULAR clinical practice guidelines for the management of PsA and their subsequent updates in 2015, as well as the 2012 BSR guidelines (due to be updated in 2017[11]), recommend the use of TNF inhibitors (such as certolizumab pegol) in certain types of patients who have had an inadequate response to only one cDMARD. For example those with
    - predominant axial disease, predominant nail involvement, dactylitis and/or predominant enthesitis;
    - poor prognostic factors.

    A summary of these recommendations is provided thereafter.
2. The UK clinical practice is highly guided by recommendations from NICE, which currently restrict the use of TNF inhibitors after inadequate response to 2 cDMARDs, thus evidence on their usage after only 1 cDMARD within the NHS is limited creating a cycle whereby formal audited data on their use is not available.
3. Previous NICE guidance has provided recommendations allowing the use of biologics in a specific subpopulation where no biologics were previously recommended (eg TA340, ustekinumab as treatment option for treating active psoriatic arthritis in adults who had treatment with 1 or more TNF–alpha inhibitors).[5]

Treatment management recommendations for use of TNF inhibitors (including certolizumab pegol) in certain types of patients with an inadequate response to only one cDMARD

PsA is a heterogeneous disease, associated with multiple and variable clinical features (in terms of both presentation and severity). Patients experience chronic inflammatory peripheral arthritis and may also suffer from skin and nail disease, axial disease, dactylitis and enthesitis.[1,2] It has been suggested that early intervention in PsA may limit damage to structural joints and produce improvements in pain and/or quality of life.[3]

Conventional DMARDs (cDMARDs), used to reduce the immunological over-reactivity seen in PsA, have little evidence to support the inhibition of structural damage progression or efficacy in patients with predominant axial disease or enthesitis.[4] Moreover as noted in TA340 by NICE: '…*conventional management with DMARDs (such as methotrexate) does not appear to provide substantial benefits for joint‑related aspects of psoriatic arthritis*.'[5] A synthetic targeted DMARD (apremilast) has also been licensed, although it has shown no significant effect on dactylitis and has no data for the effect on structural damage.[6]

TNF inhibitors, including certolizumab pegol, are efficacious[7] and have proven persistent therapeutic benefits in many areas of functional status and HRQoL, although etanercept is not considered as efficacious as other TNF inhibitors with regard to psoriatic skin involvement[8] and dactylitis.[4,9] TNF inhibitors, including certolizumab pegol, have also been shown to slow the progression of joint damage.[8,9]

Following advances in the understanding of the pathogenesis of PsA and the need to consider effective treatments that improve all disease manifestations, several treatment guidelines have been published, and subsequently updated, highlighting the important aspects to be considered when initiating a biologic or non-biologic treatments, including in patients who have failed only one cDMARD. For example:[10, 8, 4]

- BSR treatment guidelines recommend considering TNF inhibitors for a subset of patients who have failed only one DMARD where there is evidence of adverse prognostic factors;
- The international GRAPPA guideline (which also accounts for the disease severity) and the EULAR recommendations currently guide treatment of PsA and both clearly emphasize in their overarching principles the need to account for the extra articular manifestations (e.g. those with predominant axial disease, predominant nail involvement, dactylitis and/or predominant enthesitis) when managing patients with PsA.

Table 1: Summary of latest BSR, GRAPPA and EULAR treatment recommendations for PsA

Guideline	Recommendation	Further details
British Society for Rheumatology (BSR)[10]	Peripheral arthritis, (i) TNF inhibitor therapy may be considered for patients who have failed only one cDMARD where there is evidence of certain adverse prognostic factors	The guideline specifically state that these prognostic factors are: '*five or more swollen joints in association with elevated C-reactive protein persisting for >3 months or structural joint damage due to disease'*
EULAR[8]	Recommendation 5: *'In patients with peripheral arthritis and an inadequate response to at least one cDMARD, therapy with a biological DMARD, usually a TNF inhibitor, should be commenced*.' Recommendation 8: *'In patients with active enthesitis and/or dactylitis and insufficient response to NSAIDs or local glucocorticoid injections, therapy with a biological DMARD should be considered, which according to current practice is a TNF inhibitor.'* Recommendation 9: *'In patients with predominantly axial disease that is active and has insufficient response to NSAIDs, therapy with a biological DMARD should be considered, which according to current practice is a TNF inhibitor.'*	The recommendations also state: *'In patients with peripheral arthritis in whom a csDMARD (usually MTX because of its effects on joints and skin, but also leflunomide, sulfasalazine or others, see above) is not efficacious (ie, the treatment target of at least low disease activity has not been reached) even though the treatment has been taken for an appropriate length of time (usually 3–6 months), a bDMARD can be considered'* *'after failure of local or non-specific anti-inflammatory therapy, biological DMARDs may be applied even if no cDMARDs have been tried, since the latter have not been proven efficacious in treating these aspects of PsA, especially enthesitis'* *'This recommendation applies to the subgroup of patients with PsA who have predominant and active axial disease. Active disease here is usually defined in reference to a Bath Ankylosing Spondylitis Disease Activity Index above 4 points. In these patients, bDMARDs can be considered even if no csDMARDs have been tried, since csDMARDs have no proven efficacy in axial disease.'*
GRAPPA[4]	TNF inhibitors are strongly recommended for: • Peripheral arthritis, inadequate response to DMARDs • Axial PsA • Enthesitis • Dactylitis • Nail psoriasis	cDMARDs are specifically not recommended by GRAPPA in such cases of predominant extra articular manifestations.

UCB thus considers that given the heterogeneous nature of PsA and the need to effectively manage all its clinical manifestations, it is important for NICE to allow use of certolizumab pegol in a certain type of patients in cases where a second cDMARD would be ineffective and not recommended as per the above treatment guidelines. We believe that the importance of managing all the disease manifestations has also been noted in the patient and clinician submissions to the committee, and should thus be accounted for.

Furthermore, as per the UCB submitted evidence, data from the RAPID-PsA study showed that, in the subgroup of patients who are TNF inhibitor naïve and have only received one prior cDMARD (i.e. subpopulation 1), certolizumab pegol has demonstrated rapid and sustained improvements in signs and symptoms, in terms of both the joint and skin manifestations of the disease, greater improvements in physical functioning, extra-articular manifestations of disease, including nail involvement, enthesitis, dactylitis and axial involvement, as well as improvements in a broad spectrum of patient relevant outcomes (e.g. pain, fatigue, HRQoL, workplace and household productivity).

Based on the above considerations, and given the recommendations from the BSR for use of TNF inhibitors in certain types of patients with an inadequate response to only one cDMARD, together with similar recommendations from both EULAR and GRAPPA, we consider that there is a clear and consistent mandate stated in the latest clinical practice guidelines to use a TNF inhibitor in certain types of patients who have had an inadequate response to only one cDMARD and where a second cDMARD might not be an effective treatment option.

Recommendation of certolizumab pegol in certain types of patients with an inadequate response to only one cDMARD as per the EULAR and GRAPPA guidelines, would bring the NICE guidance in line with clinical practice guidelines in both the UK and Europe. This would therefore broaden the therapeutic armamentarium, with an effective treatment option for patients and clinicians, in a heterogeneous condition where it is important to manage a wide range of manifestations.

UCB thus requests that the Appraisal Committee reviews and considers the decision to withhold the recommendation of certolizumab pegol in subpopulation 1.

2 Response to topics of interest highlighted by the Appraisal Committee

2.1 Has all of the relevant evidence been taken into account?

UCB has no further comment on this point.

2.2 Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?

2.2.1 Adjustment of the placebo creep in the UCB submitted NMA

The ACD states in section 4.6, page 9 and in the Summary table on page 29 that '*The committee concluded that because these issues had either not been accounted for (secukinumab) or because it was unclear how they had been accounted for (certolizumab pegol) in the company submissions, it was not possible to make reliable conclusions about the difference in the efficacy of certolizumab pegol and secukinumab using the companies' analyses*'.

UCB would like to reiterate that this statement does not accurately reflect the evidence submitted. The occurrence of placebo creep and class effect were in fact accounted for in the analysis submitted by UCB; i.e. the adjusted meta-regression mixed treatment comparison for ACR 20/50, PASI75 and PsARC accounted for an association between the results for absolute effect in placebo arms across PsA studies identified by systematic literature review. Additionally, section 4.10 of the UCB submission states that: '*Due to the substantial level of heterogeneity on baseline risk, the results of meta-regression in TNF inhibitor naïve subpopulation presented here are based on treating [*TNF inhibitors] *as sharing a class effect (but with the possibility of variation within that class), along with controlling for baseline risk (i.e., variation in placebo response). The other biologic treatments (e.g.* [secukinumab]*) also had its odds-ratios controlled for baseline risk, but it essentially belonged to its own 'class', and thus did not 'borrow strength' from each other or any other drug.* '

The approach considered by UCB was subsequently acknowledged by the AG in their report. For example, table 131 on page 325 of the AG report summarises the key assumptions in the synthesis models for PsARC responses and states that the UCB model was '*adjusted for* [placebo response in] *the biologic naïve subpopulation*'. Furthermore, the adjusted NMA accounting for the placebo creep and class effect were used as inputs in the UCB cost-effectiveness model, which was similar to the AG approach.

UCB thus requests that the statement in the ACD is revised to accurately reflect the UCB submitted approach.

2.2.2 Summary of evidence for improvement of joint symptoms

In section 4.11 of the ACD (page 13) is stated that '*The committee concluded that although there were limitations in the analyses, it considered that certolizumab pegol and secukinumab were similar to the other therapies in improving joint symptoms in both biological-naive and experienced subpopulations*'.

UCB considers that use of the broad term 'other therapies' is not reflecting the committee meeting discussions and the clinical feedback summarized in Section 4.11, which was referring to TNF alpha inhibitors. We request that the text be amended to (revision underlined): '*The committee concluded that although there were limitations in the analyses, it considered that certolizumab pegol and secukinumab were similar to <u>TNF alpha inhibitors</u> in improving joint symptoms in both biological-naive and experienced subpopulations*'.

2.2.3 Summary of safety profiles

In Section 4.12, page 13 of the ACD, it has been stated that: '…..*there was no concern about additional adverse events for certolizumab pegol and secukinumab over other biological therapies. The committee concluded that the safety profiles of certolizumab pegol and secukinumab were comparable*'.

UCB requests that the statement be revised to correctly specify the appropriate comparison being referred to, as per the committee meeting discussions (suggested revision underlined): '*there was no*

concern about additional adverse events for certolizumab pegol and secukinumab over other TNF inhibitors. The committee concluded that the safety profiles of certolizumab pegol and secukinumab were comparable to the other TNF inhibitors'.

2.3 Are the recommendations sound and a suitable basis for guidance to the NHS?

- Section 4.2, page 8 of the ACD indicates that '*The committee heard from the clinical experts that both certolizumab pegol and secukinumab 300mg were effective therapies and that secukinumab was particularly effective in severe psoriasis*.' UCB considers that this summary of the clinical experts' opinion is unclear given that the focus of the guidance should be on the joints rather than skin. Therefore, UCB requests that the text be revised to indicate (revision underlined): '…*that secukinumab 300mg was particularly effective in treating symptoms of psoriasis in PsA patients with severe psoriasis*.'

- Section 4.10, page 12 of the ACD states '*The clinical experts agreed that patients with early primary treatment failure would respond differently to a subsequent second biological therapy (that is, TNF-alpha inhibitors*).' UCB considers that this statement does not accurately reflect the clinical expert input during the first Appraisal Committee meeting and requests that the statement be revised to (text underlined): '*The clinical experts agreed that patients with primary treatment failure would respond differently to a subsequent second biological therapy (that is, TNF-alpha inhibitors) than patients who had not previously experienced primary failure*.'

2.4 Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?

UCB has no comment on this point.

3 Factual inaccuracies

A summary of the factual inaccuracies included in the document is provided in Table 2.

Table 2: Summary of factual inaccuracies in the ACD

Page	Content from the ACD report	UCB comment
3	Paragraph 1.1 of the ACD states: '*Certolizumab pegol is only recommended if the company provides it agreed in the patient access scheme*.'	Revision underlined: '*Certolizumab pegol is only recommended if the company provides it as agreed in the approved patient access scheme*'
3	Paragraph 1.2 of the ACD states: *'Secukinumab alone, or in combination with methotrexate, is recommended as an option for treating active psoriatic arthritis in adults only if:* • *it is used as described in the NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis (recommendations 1.1 and 1.2) or* • *the person has had a TNF-alpha inhibitor but their disease has not responded within the first 12 weeks or has stopped responding after 12 weeks or* • *TNF-alpha inhibitors are contraindicated but would otherwise be considered (as described in NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis)*.'	This recommendation is incomplete as it omits the fact that secukinumab is only licensed for use in patients who have already received biologic therapies at a dose of 300mg (see section 4.18 of the ACD). UCB therefore requests that NICE amend the wording in line with the approved posology of secukinumab. The text should be amended to (revision underlined): '*Secukinumab alone, or in combination with methotrexate, is recommended as an option for treating active psoriatic arthritis in adults only if:* • *it is used as described in the NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis (recommendations 1.1 and 1.2) or* • *[at the 300mg dose] the person has had a TNF-alpha inhibitor but their disease has not responded within the first 12 weeks or has stopped responding after 12 weeks or* • *TNF-alpha inhibitors are contraindicated but would otherwise be considered (as described in NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis)*.'
6	In Section 2 of the ACD (Price) it is stated: '*The company has agreed a patient access scheme with the Department of Health. The first 12 weeks of therapy with certolizumab pegol will be free of charge.*'	This statement is incomplete and the following text should be added (revision underlined): '*The company has agreed a patient access scheme with the Department of Health. The first 12 weeks of therapy with certolizumab pegol will be free of charge. The Department of Health considered that this patient access scheme does not constitute an excessive administrative burden on the NHS*'
17 and 22	In Section 4.18 and in the summary table of the ACs key conclusions, subpopulation 3 is referred to as: '*Subpopulation 3: patients who have had biological therapies*'	The subpopulation definition should be amended to (revision underlined): '*Subpopulation 3: patients who have had TNF-alpha inhibitors'*
23	The summary table of the ACs key conclusions contains the following: '*People with psoriatic arthritis whose disease has not responded adequately to 2 DMARDs and whose disease has not responded adequately to DMARDs*'	The statement contains a duplication and should be revised to: '*People with psoriatic arthritis whose disease has not responded adequately to 2 DMARDs*'
32-33	The ACD states that: '*The committee concluded that certolizumab pegol is cost effective in 2 subpopulations….with ICERs below, or close to, £20,000 per QALY gained when taking into account the proposed patient access scheme for certolizumab pegol'*	Given that the PAS for certolizumab has been agreed with the Department of Health, we would request the text to be amended as follows (revision underlined): '*The committee concluded that certolizumab pegol is cost effective in 2 subpopulations….with ICERs below, or close to, £20,000 per QALY gained when*

Page	Content from the ACD report	UCB comment
		taking into account the approved patient access scheme for certolizumab pegol'
35	In Section 5.4 of the ACD the approved PAS for certolizumab pegol is summarised as: '…..*The Department of Health and UCB have agreed that a patient access scheme for certolizumab pegol which provides a rebate to the list price of certolizumab pegol, applied at the point of purchase or invoice. The NHS will not pay for certolizumab pegol for the first 12 weeks. The size of these discounts is commercial in confidence. It is the responsibility of the companies to communicate details of the discount to the relevant NHS organisations*.'	The text inaccurately implies that the certolizumab pegol PAS is a discount and that it is commercial in confidence. We would thus request the following revisions (text underlined) to ensure clarity in the description of the PAS: '*The Department of Health and Novartis have agreed that secukinumab will be available to the NHS with a patient access scheme which makes it available with a discount*. *The size of the discount is commercial in confidence*. *The Department of Health and UCB Pharma have agreed that certolizumab pegol will be available to the NHS with a patient access scheme. UCB Pharma will provide the first 12 weeks of certolizumab pegol free of charge, which is equivalent to 10 vials*. *It is the responsibility of the companies to communicate details of the discount/patient access scheme to the relevant NHS organisations*.'

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2. Ritchlin CT, Kavanaugh A, Gladman DD, Mease PJ, Helliwell P, Boehncke WH, de Vlam K, Fiorentino D, et al. Treatment recommendations for psoriatic arthritis. *Annals of the Rheumatic Diseases.* Sep 2009;68(9):1387-1394.

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11. The Brisitsh Society of Rheumatology (http://www.rheumatology.org.uk/resources/guidelines/) Accessed 27-01-2017.

24 January 2017

National Institute for Health and Care Excellence

Single Technology Appraisal

Psoriatic arthritis: certolizumab pegol and secukinumab (after DMARDs) [ID579]

AbbVie's response to ACD2

24 January 2017

Dear Meindert,

AbbVie welcomes the opportunity to comment on the second Appraisal Consultation Document (ACD2) for the single technology appraisal (STA) of certolizumab pegol and secukinumab (after DMARDs) in psoriatic arthritis [ID579].

Please find AbbVie's comments below, for your consideration.

With kind regards

[redacted], AbbVie UK Ltd.

Comment 1

Section 1.3, page 3 of the ACD2 contains the statement "Assess the response to certolizumab pegol and secukinumab after 12 weeks and 16"

AbbVie is particularly concerned that this statement is going to introduce an unwarranted level of complexity in clinical practice, with the risk that some patients may unnecessarily be delayed in their subsequent disease assessment if two thresholds (of 12 and 16 weeks) are recommended.

Comment 2

Section 4.1 of the ACD2, page 7

AbbVie believes that the following sentence: "The committee heard from the clinical experts that psoriatic arthritis not only affects joints and tendons but can also be associated with other debilitating conditions of the skin, bowel and eye and with metabolic syndrome." should be followed by: "The Committee recognizes that secukinumab has not demonstrated clinical effectiveness in inflammatory bowel disease".

Comment 3

Section 4.2 of the ACD2, page 8

AbbVie believes that the sentence "The clinical experts commented that certolizumab pegol targets TNF-alpha and that secukinumab has a different mechanism of action, targeting interleukin 17A (IL-17A), which could potentially benefit people in whom TNF-alpha inhibitors are contraindicated or not tolerated" should be followed by a statement clarifying that TNF-alpha are the preferred first-line biologic agents.

24 January 2017

Comment 4

Section 4.11 of the ACD2, pages 12-13

Abbvie wishes to highlight that psoriatic arthritis is a multi-faceted disease composed of arthritis, psoriasis and extra-articular manifestations/ comorbidities such as Inflammatory bowel disease. The Appraisal Committee should take into consideration the study by Hueber et al (2012), and, after the sentence: “The clinical experts stated that they could not distinguish between the TNF-alpha inhibitors in improving joint symptoms in clinical practice and would therefore choose 1 of the therapies based on availability and the patient’s comorbidities”, it should include the statement “Secukinumab has failed to demonstrate clinical effectiveness in the extra-articular component of psoriatic arthritis, as demonstrated in patients with Crohn’s disease”.

Reference

Hueber W, et al. “Secukinumab, a human anti-IL-17A monoclonal antibody, for moderate to severe Crohn's disease: unexpected results of a randomised, double-blind placebo-controlled trial”; Gut. 2012 Dec;61(12):1693-700. doi: 10.1136/gutjnl-2011-301668. Epub 2012 May 17.

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Celgene Comments on the second Appraisal Consultation Document (ACD) for CZP and SEC for PsA: NICE MTA [ID579]

Celgene welcomes the opportunity to comment on the second Appraisal Consultation Document (ACD) for certolizumab pegol (CZP) and secukinumab (SEC) for active PsA [ID579].

Celgene has one area of comment:

1. **Celgene agrees with the Committee's decision not to recommend CZP and SEC in sub population 1 (biologic-naïve patients who have received one prior DMARD)**

According to NICE guidance (TA199,[1] TA220[2]), the NICE commissioning algorithm for biologic drugs for the treatment of psoriatic arthritis,[3] and the British Society for Rheumatology 2012 guidelines,[4] the biologic agents adalimumab, etanercept, infliximab and golimumab are recommended in patients who have not responded to adequate trials of at least **two** standard DMARDs, administered either individually or in combination. Accordingly, if the cost-effectiveness of CZP and SEC is to be considered in subpopulation 1, Celgene considers that the appropriate comparator, i.e. a **second non-biologic DMARD (and not Best Supportive Care)**, should be used to reflect routine NHS practice. This would also be consistent with the Final Scope for this appraisal which lists the following comparators:

For people who have only received 1 prior non-biological disease modifying anti-rheumatic drug (DMARD)

- *Disease modifying anti-rheumatic drugs*

For people whose disease has not responded adequately to at least 2 DMARDs:

- *Biological therapies (with or without methotrexate including etanercept, adalimumab, infliximab, golimumab, apremilast [subject to ongoing NICE appraisal]),*

For people whose disease has not responded adequately to DMARDs and not adequately responded to biological therapies (including etanercept, adalimumab, infliximab and golimumab) or biological therapies are contraindicated:

- *Ustekinumab*
- *Apremilast [subject to ongoing NICE appraisal]*
- *Best supportive care.*

Additionally, Celgene notes that the marketing authorization for CZP and SEC is aligned to that of other biologics licensed for psoriatic arthritis and considers that a similar approach to evaluating their use on the NHS should be taken to ensure consistency with previous NICE appraisals (TA199, TA220).
Celgene notes that the York AG makes similar reference when discussing limitations of their analyses (Assessment Report p.248-9):

"…subpopulation 1 only includes the comparators CZP, SEC and BSC, as per the NICE scope. It is recognised however, that there may be other comparators relevant for this subpopulation. In particular, patients who have only received 1 prior DMARD may be eligible to receive a 2nd DMARD. It was not possible within the scope of this appraisal to assess the evidence for DMARDs and therefore include this as a formal comparator in this subpopulation. The extremely low cost of DMARDs (7.5 mg of MTX is £0.30) make it likely that these would be considered cost-effective in this population…"

Celgene notes that the AG have stated that BSC is listed as a comparator for sub population 1 however this is not consistent with the final scope for this appraisal for which BSC is only included as a comparator for people whose disease has not responded adequately to DMARDs and not adequately responded to biological therapies (including etanercept, adalimumab, infliximab and golimumab) or biological therapies are contraindicated.

In the first ACD, the Committee noted:

"For subpopulation 1 (1 previous DMARD but no biological therapy), the committee noted that the comparators in the assessment group's model and the group represented by the biological-naive subpopulation did not reflect clinical practice in England. For these reasons, the committee concluded that certolizumab pegol and secukinumab could not be recommended as treatment options for people with psoriatic arthritis whose disease had not responded adequately to 1 DMARD."

Celgene agrees with the provisional recommendations made in the ACD not to recommend CZP and SEC in patients that are biologic-naïve who have received one prior DMARD. The manufacturers have not submitted analyses comparing against the relevant comparator in routine NHS practice, a second non-biologic DMARD, and it is highly unlikely that either of these technologies would be considered cost-effective at this stage in the pathway based on the comments made by the York AG.

Celgene considers that, should the Committee wish to evaluate SEC and CZP in sub population 1, this should take place alongside a review of existing NICE Guidance for recommended technologies for PsA to ensure a consistent approach.

Comments on the additional analysis submitted by Novartis in sub population 1

During consultation, Novartis have submitted an additional cost-effectiveness analysis for sub population 1. Celgene considers this analysis to be flawed for a number of reasons, with a high degree of uncertainty and should therefore be interpreted with extreme caution. Whilst the additional clinical data used for SEC from FUTURE 2 appears to be more relevant to sub population 1, the comparator efficacy data used in this analysis is not appropriate, for the following reasons:

1. The NICE final scope for this appraisal states that a second DMARD and **not** BSC is the appropriate comparator in this population (see above).
2. FUTURE 2 is not an active comparator study and compares SEC versus placebo. The placebo arm of the SEC FUTURE 2 trial is likely to underestimate the efficacy of the appropriate comparator in this position and favour SEC in the analysis.
3. No attempt to assess the clinical evidence for DMARDs in this sub population has been made by the manufacturer (or the AG) resulting in a high degree of uncertainty.

In the second ACD, the Committee comment (section 4.16):
"The committee heard from the assessment group that the analysis done by Novartis only included secukinumab and best supportive care and therefore was lacking the full comparator set for subpopulation 1, in particular the other biological treatments (etanercept, infliximab, adalimumab and golimumab), which according to their licences could be used in subpopulation 1."

Celgene agrees with the Committee comments that the full range of comparators may not have been included for sub population 1, but does not agree that the important omission relates primarily to TNF-alpha inhibitors. Based on expert opinion, TNF-alpha inhibitors are not routinely used after 1 DMARD in NHS practice as existing NICE Guidance (TA199 and TA220) restricts reimbursement to after 2 or more DMARDs.

Celgene considers that the most important omission in the Novartis analysis relates to the exclusion of a second DMARD as a formal comparator in this sub population. Until the manufacturer is able to assess the clinical evidence for the use of a DMARD in this sub population through a systematic literature review, and present the cost-effectiveness results in a fully incremental analysis relative to the full comparator set, there remains a high degree of uncertainty with the company conclusions. It would not be sufficient to simply include the TNF-alpha inhibitors as comparators in this sub population as this would still lack the second DMARD, which is most relevant to routine NHS practice. As stated previously, modelling BSC and using the

PBO arm from the SEC trials to inform the efficacy introduces a significant amount of uncertainty and is not considered appropriate for this comparison.

Celgene also notes that the current recommendations for SEC made by the Scottish Medicines Consortium (SMC) in July 2016 are restricted and do not include sub population 1.[i]

In summary, neither manufacturer have presented sufficiently robust cost-effectiveness evidence versus a second DMARD to justify a recommendation in sub population 1 and Celgene agrees fully with the Committee's provisional "not recommended" in this population.

Kind regards,

[redacted]

[redacted]

References:

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[i] https://www.scottishmedicines.org.uk/files/advice/secukinumab_Cosentyx__sA_FINAL_July_2016_for_website.pdf (accessed Jan 2017)

Certolizumab Pegol and secukinumab for treating active psoriatic arthritis after inadequate response to DMARDs

To whom it may concern,

The Psoriasis Association welcomes the positive recommendations for use of certolizumab pegol and secukinumab to treat psoriatic arthritis, providing eligibility criteria is met.

Psoriatic arthritis can affect people of any age, and often it affects people in young or 'mid' adulthood who should, otherwise, be 'in their prime', pursuing careers, relationships and families. Crucially, without timely and effective treatment, the damage – and associated symptoms and impacts – caused by psoriatic arthritis can be permanent. Both of these treatments work to modify the disease itself, and also work in a different manner to the currently-available anti-TNFs, meaning they are both useful options for people who may not have experienced adequate results with anti-TNFs, or cannot take them.

We have no other comment to make on the Appraisal Consultation Document, other than to reiterate our support once again for the positive recommendation of certolizumab pegol and secukinumab for psoriatic arthritis.

Yours faithfully,

[redacted]

[redacted]

Psoriasis Association