**National Institute for Health and Care Excellence**

**Single Technology Appraisal (STA/MTA)**

# Secukinumab for treating ankylosing spondylitis after inadequate response to non-steroidal anti-inflammatory drugs or TNF-alpha inhibitors

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

**Comment 1: the draft remit**

| Section | Consultee/ Commentator | Comments | Action |
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| Appropriateness | National Ankylosing Spondylitis Society | NASS believe it would be appropriate for this topic to be referred to NICE for appraisal.<br><br>200,000 people in the UK are estimated to suffer with ankylosing spondyliis (AS) in the UK. Conventional therapies for AS are limited to non-steroidal anti-inflammatory drugs (NSAIDs) and exercise. If NSAIDs fail patients can move to one anti TNF option under current NICE guidance. We know that anti TNF therapy is effective for approximately 8 in 10 patients, but for the 2 in 10 patients who fail or who cannot tolerate the side effects there are currently no further options.<br><br>Additionally, registry data indicates that, for some patients, effectiveness of anti TNF therapy can wane over time. The data shows that sequential treatment with anti TNF can be worthwhile but the drug survival, response rates and benefits appear to be reduced with the second and third anti TNFs. Thus there is a clear need for another therapy for AS patients.<br><br>This topic would address an issue which is a priority. | Comments noted. No changes to the scope are required. |
| | Novartis | Yes we consider this appraisal to be appropriate. | Comment noted. No |

| Section | Consultee/ Commentator | Comments | Action |
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| | | | changes to the scope are required. |
| | Pfizer | The remit of this appraisal appears appropriate. | Comments noted. No changes to the scope are required. |
| Wording | National Ankylosing Spondylitis Society | Yes | Comment noted. No changes to the scope are required. |
| | Novartis | [redacted] However, we agree that it will be appropriate to consider two populations separately within the appraisal;<br>• Those for whom non-steroidal anti-inflammatory drugs have been inadequately effective or not tolerated<br>• Those for whom TNF-alpha inhibitors have been inadequately effective or not tolerated | Comments noted. The population section in the scope has been updated to remove the term 'moderate' and 'severe'. The population is now as follows: 'adults with active ankylosing spondylitis for whom non-steroidal anti-inflammatory drugs, or TNF-alpha inhibitors have been inadequately effective or not tolerated.'<br>The 'Other considerations' section of the scope has been |

| Section | Consultee/ Commentator | Comments | Action |
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| | | | updated to include the suggested subgroups:<br>'If evidence allows, the appraisal should consider people who have or have not had TNF-alpha inhibitors. |
| | Pfizer | No comments | No changes required to the scope. |
| Timing Issues | National Ankylosing Spondylitis Society | NASS believe that this topic should be treated as urgent. AS usually begins in early adulthood, a critical period in terms of education, work and establishment of social frameworks and relationships.<br>Since anti TNF therapy was approved by NICE in 2009 it has made a very significant difference to the lives of many with AS. However, a significant proportion remain in whom NSAIDs or anti TNF therapies have not been tolerated, inadequately effective or where efficacy has waned over time. | Comments noted. NICE aims to produce guidance on the use of new technologies within 6 months of the approval of their marketing authorisation or launch (whichever is later). NICE can only begin to appraise a technology when it has been formally referred by the Secretary of State for Health. Following referral, NICE will schedule this topic into the work programme as soon as |

| Section | Consultee/ Commentator | Comments | Action |
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| | | | it is possible. |
| | Novartis | Secukinumab offers a novel mechanism of action for the treatment of ankylosing spondylitis in this area of high unmet need. We therefore believe secukinumab should be reviewed promptly by NICE following marketing authorisation. | Comment noted. NICE aims to produce guidance on the use of new technologies within 6 months of the approval of their marketing authorisation or launch (whichever is later). NICE can only begin to appraise a technology when it has been formally referred by the Secretary of State for Health. Following referral, NICE will schedule this topic into the work programme as soon as it is possible. |
| | Pfizer | No comments | No changes to the scope required. |
| Additional comments on the draft remit | National Ankylosing Spondylitis Society | No. | No changes to the scope required. |

| Section | Consultee/ Commentator | Comments | Action |
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| | Novartis | No comment. | No changes to the scope required. |
| | Pfizer | No comment. | No changes to the scope required. |

**Comment 2: the draft scope**

| Section | Consultee/ Commentator | Comments | Action |
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| Background information | National Ankylosing Spondylitis Society | None. | No changes to the scope required. |
| | Novartis | The impact of severe ankylosing spondylitis on health-related quality of life is not mentioned and can be considerable, with some patients becoming severely disabled due to the bones in their spine fusing in a fixed position and damage to other joints, such as the hips or knees (http://www.nhs.uk/conditions/Ankylosing-spondylitis/Pages/Introduction.aspx).<br><br>The impact of ankylosing spondylitis on work productivity is an important aspect of the condition that is not currently covered in the background section. Over half of people living with severe AS identified work as the area of their lives most affected by their condition, according to the results of a survey published by the National Ankylosing Spondylitis Society in 2009 (http://nass.co.uk/silo/files/media-release-working-with-as.pdf) In 2013, musculoskeletal conditions were the main cause for working days lost | Comment noted. The background section of the scope is only intended to provide a brief overview of the condition and current treatment options. A more detailed description of the nature of the condition will be included in the company's evidence submission during the |

| Section | Consultee/ Commentator | Comments | Action |
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| | | (http://www.ons.gov.uk/ons/rel/lmac/sickness-absence-in-the-labour-market/2014/sty-sickness-absence.html). We query whether it is relevant to include the first sentence of the third paragraph since "documented radiologic evidence (X-ray) fulfilling the Modified New York criteria for AS" formed part of the Phase III study inclusion criteria. Hence those with "non-radiographic" disease will not be [redacted] relevant to the appraisal. | course of the appraisal.<br>Following advice from consultees the following sentence has been included in the background section of the scope: 'Biosimilar versions of infliximab (Remsima, Celltrion Healthcare; Inflectra, Hospira) have been licensed for the same indications.' |
| | Pfizer | No comments. | No changes to the scope required. |
| The technology/ intervention | National Ankylosing Spondylitis Society | Yes. | No changes to the scope required. |
| | Novartis | [redacted] The statement "Secukinumab does not have a marketing authorisation in the UK" is no longer accurate unless it is made specific to the ankylosing spondylitis indication. The European Commission approved Cosentyx (secukinumab) for first-line systemic treatment of moderate-to-severe plaque psoriasis on January 15th | Comment noted. The technology section of the scope has been amended to specify that secukinumab does not have a marketing authorisation in the UK for treating ankylosing |

| Section | Consultee/ Commentator | Comments | Action |
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| | | 2015. | spondylitis. |
| | Pfizer | No comments | No changes to the scope required. |
| Population | National Ankylosing Spondylitis Society | No comments | No changes to the scope required. |
| | Novartis | [redacted]<br><br>The population studied within the secukinumab Phase III studies (MEASURE1: NCT01358175 / CAIN457F2305 and MEASURE 2: NCT01649375 / CAIN457F2310) were "Male and female patients aged at minimum 18 at time of consent, with moderate to severe AS fulfilling the Modified New York criteria for ankylosing spondylitis with prior documented radiological evidence (X-ray or radiologist's report). Patients must have a history of active AS and a BASDAI ≥4 (0-10) and spinal pain as measured by visual analogue scale (VAS) ≥4 cm, on a scale of 0-10 cm."<br><br>The study populations were stratified according to being TNF-alpha inhibitor incomplete responders (TNF-IR) or TNF-alpha inhibitor naive patients.<br><br>In MEASURE1, 73% of patients were naïve to TNF-alpha inhibitors (n=271/371). In MEASURE 2, 62% of patients were naïve to TNF-alpha inhibitors (n=135 / 219). | Comments noted. Consultees at the scoping workshop agreed that the population in the scope should be amended to remove the term 'moderate'. The population in the scope has been amended to 'adults with active ankylosing spondylitis for whom non-steroidal anti-inflammatory drugs, or TNF-alpha inhibitors have been inadequately effective or not tolerated.' |

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| | Pfizer | Pfizer suggest that the definition of disease severity be consistent with that used in previous and ongoing NICE appraisals of anti-TNFs for the treatment of ankylosing spondylitis (ie severe disease, not moderate to severe) (1-3).<br><br>References:<br>1. National Institute for Health and Clinical Excellence. Adalimumab, etanercept and infliximab for ankylosing spondylitis. May, 2008. NICE technology appraisal guidance 143. Available from: http://www.nice.org.uk/nicemedia/pdf/TA143Guidance.pdf (Accessed February, 2015).<br>2. National Institute for Health and Clinical Excellence. Golimumab for the treatment of ankylosing spondylitis. NICE technology appraisal guidance 233. August 2011. Available from: https://www.nice.org.uk/guidance/ta233 (Accessed February, 2015)<br>3. National Institute for Health and Clinical Excellence. Ankylosing spondylitis and axial spondyloarthritis (non-radiographic) - adalimumab, etanercept infliximab and golimumab (inc rev TA143 and TA233) Final scope May, 2014. Available from: http://www.nice.org.uk/guidance/gid-tag355/documents/ankylosing-spondylitis-and-axial-spondyloarthritis-nonradiographic-adalimumab-etanercept-infliximab-and-golimumab-inc-rev-ta143-and-ta233-final-scope-2. (Accessed February, 2015) | Comments noted. Consultees at the scoping workshop agreed that the population in the scope should be amended to remove the term 'moderate'. The population in the scope has been amended to 'adults with active ankylosing spondylitis for whom non-steroidal anti-inflammatory drugs, or TNF-alpha inhibitors have been inadequately effective or not tolerated.' |
| Comparators | Merck Sharpe and Dohme | The NICE commissioning algorithm for biologic drugs for the treatment of ankylosing spondylitis indicates that for patients who are intolerant to TNF inhibitors within the first 12 weeks another TNF inhibitor can be considered. Therefore, for patients who are intolerant to TNF inhibitors the comparators for secukinumab should include other TNF inhibitors.<br><br>If the patient has primary non-response to a TNF inhibitor, the commissioning algorithm states that the patient should discontinue treatment. It is not clear | Comments noted. The proposed technology appraisal can only consider secukinumab within its proposed marketing authorisation. Therefore, any comparisons can only |

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| | | whether clinicians would use another TNF inhibitor in cases of secondary non-response (i.e. loss of response) prior to secukinumab. If so, the comparators for secukinumab should include other TNF inhibitors. | be made with technologies that are currently used in the relevant population. No changes to the scope required. |
| | National Ankylosing Spondylitis Society | No comments | No changes to the scope required. |
| | Novartis | Yes, we consider these to be the appropriate comparators for each sub-group. We would suggest a small change to the wording “or who are intolerant” rather than “or is intolerant”. | Comment noted. The scope has been updated accordingly. |
| | Pfizer | Certolizumab pegol is currently subject to an ongoing NICE multiple technology appraisal that includes patients with ankylosing spondylitis (1).<br><br>References:<br>1. National Institute for Health and Clinical Excellence. Adalimumab, etanercept and infliximab for ankylosing spondylitis. May, 2008. NICE technology appraisal guidance 143. Available from: http://www.nice.org.uk/nicemedia/pdf/TA143Guidance.pdf (Accessed February, 2015). | Comment noted. Certolizumab pegol has been included as a comparator in the scope. |
| Outcomes | National Ankylosing Spondylitis | Yes. | Comment noted. No changes to the scope required. |

| Section | Consultee/ Commentator | Comments | Action |
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| | Society | | |
| | Novartis | We consider the specified outcome measures to be appropriate. The secukinumab Phase III studies (MEASURE 1 and MEASURE 2) assessed disease activity using BASDAI (Bath Ankylosing Spondylitis Disease Activity Index), ASAS (Assessment in Spondylo Arthritis Core set) and ASDAS (Ankylosing Spondylitis Disease Activity Assessment). In both studies functional capacity was assessed by BASFI (Bath Ankylosing Spondylitis Functional Index). In both studies spinal mobility was assessed by BASMI (Bath Ankylosing Spondylitis Metrology Index). In both studies disease progression was assessed using the 44-joint assessment for tender or swollen joints, ESR and hsCRP. Additionally in MEASURE 1 disease progression was assessed by X-ray of the cervical, thoracic and lumbar spine assessed by modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS), MRI of spine and sacroiliac joints and DXA of the lumbar spine, total hip and femoral neck. In both studies peripheral symptoms were assessed using MASES (Expanded Maastricht Ankylosing Spondylitis Enthesitis Score). In both studies health-related quality of life was assessed using EQ-5D, SF-36, ASQoL and FACIT-Fatigue. | Comments noted. No changes to the scope required. |
| | Pfizer | No comments | No changes to the scope required. |
| Economic analysis | National Ankylosing Spondylitis Society | No comments | No changes to the scope required. |
| | Novartis | No comment. | No changes to the scope required. |

| Section | Consultee/ Commentator | Comments | Action |
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| | Pfizer | No comments | No changes to the scope required. |
| Equality and Diversity | National Ankylosing Spondylitis Society | No comments | No changes to the scope required. |
| | Novartis | No comment. | No changes to the scope required. |
| | Pfizer | No comments | No changes to the scope required. |
| Innovation | National Ankylosing Spondylitis Society | This is an innovative technology and has the potential to make a substantial impact on the way in which AS is managed. | The Committee will consider the innovative nature of secukinumab for ankylosing spondylitis during the course of the appraisal. No changes to the scope required. |
| | Novartis | Secukinumab offers a novel mechanism of action for the treatment of ankylosing spondylitis; targeting IL 17A and inhibiting its interaction with the IL 17 receptor.<br>Ankylosing spondylitis typically affects young people, with onset typically occurring in the late teenage years and twenties and it is nearly three times more common in men than in women (http://nass.co.uk/silo/files/media- | The Committee will consider the innovative nature of secukinumab for ankylosing spondylitis during the course of the appraisal. No changes to the |

| Section | Consultee/ Commentator | Comments | Action |
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| | | release-working-with-as.pdf). As such, there will be indirect benefits of treatment (such as work productivity) that will not be included in the QALY calculation. The secukinumab phase III studies (MEASURE 1 and MEASURE 2) captured work productivity benefits via the WPAI-GH (Work Productivity and Activity Impairment - General Health). | scope required. |
| | Pfizer | No comments | No changes to the scope required. |
| Other considerations | National Ankylosing Spondylitis Society | No comments. | No changes to the scope required. |
| | Novartis | No comment. | No changes to the scope required. |
| | Pfizer | No comments | No changes to the scope required. |
| Questions for consultation | Merck Sharpe and Dohme | Certolizumab pegol is included in the ongoing NICE MTA for ankylosing spondylitis and axial spondyloarthritis.<br>Biosimilar infliximab has a marketing authorisation for ankylosing spondylitis and will be marketed in the UK from the 25th February 2015; however, originator infliximab (Remicade) has not been reimbursed by NICE for ankylosing spondylitis. | Comments noted. Certolizumab pegol has now been included as a comparator in this proposed technology appraisal. |
| | National Ankylosing Spondylitis | No comments. | No changes to the scope required. |

| Section | Consultee/ Commentator | Comments | Action |
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| | Novartis | Which treatments are considered to be established clinical practice in the NHS for ankylosing spondylitis?<br>Is certolizumab pegol used in clinical practice for treating adults with radiologic evidence (X-ray) of moderate to severe ankylosing spondylitis?<br>Specialist Share Data from NHiS indicates that in September 2014 UK biologic patient shares in Ankylosing Spondylitis were as follows:<br>[redacted]<br>On this basis we do not believe that certolizumab pegol should be included as a comparator within this appraisal.<br>Are there any biosimilar drugs with a marketing authorisation in this therapeutic indication?<br>Although biosimilar infliximab has been approved by the EMA, it is not yet available in the UK. Since biosimilars are not established clinical practice in the UK they should not be included as comparators within this appraisal.<br>Are there any subgroups of people in whom secukinumab is expected to be | Comments noted. Certolizumab pegol has been included as a comparator technology in this proposed technology appraisal because it is being considered as part of the ongoing NICE multiple technology appraisal review for ankylosing spondylitis and axial spondyloarthritis ID694].<br>Comment noted. NICE technology appraisals will use the name of the active drug substance, including reference products and brand named similar biological medicinal products in its |

| Section | Consultee/ Commentator | Comments | Action |
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| | | more clinically effective and cost effective or other groups that should be examined separately?<br>See earlier comments on "Population" relating to TNF-alpha inhibitor incomplete responders (TNF-IR) versus TNF-alpha inhibitor naive patients.<br>Where do you consider secukinumab will fit into the existing NICE pathway for 'musculoskeletal conditions'?<br>Pending the outcome of this appraisal we would envisage that secukinumab will fit within the "Ankylosing spondylitis" section of the "Musculoskeletal conditions" NICE pathway. | documentation where appropriate to inform clinical decision making and to reflect the remit received from Ministers.<br>Comment noted. No changes to the scope required. |
| | Pfizer | No comments | No changes to the scope required. |
| Additional comments on the draft scope | AbbVie | It is important that the draft scope is in line with that agreed for the ongoing MTA of TNF inhibitors for the treatment of ankylosing spondylitis, except where the licensed indication differs. | Comment noted. |
| | National Ankylosing Spondylitis Society | No comments. | No changes to the scope required. |
| | Novartis | No comment. | No changes to the scope required. |

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

Department of Health
Royal College of Pathologists

**NATIONAL INSTITUTE FOR HEALTH CLINICAL EXCELLENCE**

**Single Technology Appraisal (MTA) (STA)**

**Secukinumab for treating ankylosing spondylitis after inadequate response to non-steroidal anti-inflammatory drugs or TNF-alpha inhibitors**

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

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| **Version of matrix of consultees and commentators reviewed:**<br>Provisional matrix of consultees and commentators sent for consultation | | | | | |
| **Summary of comments, action taken, and justification of action:** | | | | | |
| | Proposal: | Proposal made by: | | Action taken:<br>Removed/Added/Not included/Noted | Justification: |
| 1. | Afiya Trust | NICE Secretariat | | Removed | This organisation is no longer active. Afiya Trust has been removed from the matrix of consultees and commentators under 'patient/carer group' |

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| 2. | Equalities National Council | NICE Secretariat | | Removed | This organisation's interests are not related to the appraisal topic and as per our inclusion criteria. Equalities National Council has been removed from the matrix of consultees and commentators under 'patient/carer groups' |
| 3. | Muslim Health Network | | | Removed | This organisation no longer exists. Muslim Health Network has been remove from the matrix of consultees and commentators under 'patient/carer groups'. |