National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Secukinumab for treating non-radiographic axial spondyloarthritis ID1419

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

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

Comment 1: the draft remit

Section	Consultee/ Commentator	Comments [sic]	Action
Appropriateness	British Society for Rheumatology	Yes	Comment noted.
	National Ankylosing Spondylitis Society	NASS believes that it is appropriate for this topic to be referred to NICE for appraisal. It is estimated that 1 in 200 of the adult population in the UK have axial spondyloarthritis (axial SpA). Currently NSAIDs and exercise are the conventional treatment for non-radiographic axial SpA. If NSAIDs fail, under current NICE guidance, people with radiographic axial SpA, also known as ankylosing spondylitis (AS) can access TNF-alpha inhibitors adalimumab, certolizumab pegol, etanercept, golimumab and infliximab, followed by IL17a inhibitor secukinumab as treatment. People with non-radiographic axial SpA can access adalimumab, certolizumab pegol, etanercept, golimumab as treatment options.	Comment noted.

Section	Consultee/ Commentator	Comments [sic]	Action
		Evidence shows that the effectiveness of TNF-alpha inhibitors can wear off over time and under current NICE guidance (383) patients with non-radiographic axial SpA are able to switch to another TNF-alpha inhibitor NASS welcomes an IL17-A inhibitor to be considered for non-radiographic axial SpA to further enhance treatment options.	
	Novartis	We consider the proposed appraisal appropriate.	Comment noted.
Wording	British Society for Rheumatology	Yes	Comment noted.
	National Ankylosing Spondylitis Society	Yes	Comment noted.
	Novartis	We consider the proposed appraisal appropriate.	Comment noted.
Timing Issues	British Society for Rheumatology	No immediate urgency as other treatments currently available	Comment noted.
	National Ankylosing Spondylitis Society	NASS believes that this topic should be treated as moderately urgent. Axial SpA usually begins in early adulthood, a critical period in terms of education, work and establishment of social relationships. Since biologic therapy was approved by NICE it has made a very significant difference to the lives of many with axial SpA. However, NSAIDs or anti TNF therapies are not tolerated, inadequately effective or where efficacy has waned over time in a significant amount of the population. An IL17-A as an	Comment noted. The aim of the STA process is to provide guidance close to the MA being granted.

Section	Consultee/ Commentator	Comments [sic]	Action
		alternative to other biologic therapies following failure using NSAIDs is welcomed.	
	Novartis	Secukinumab offers a novel mechanism of action for the treatment of non-radiographic axial spondyloarthritis (nr-axSpA). The health-related quality of life impact of nr-axSpA is similar to ankylosing spondylitis (also known as radiographic axSpA), with comparable patient self-reported disease activity and functional impairments.1 Furthermore, since nr-axSpA is typically diagnosed amongst people in their 30's,2 work impairment is considerable, both in terms of withdrawal from work (including early retirement) and work instability, with consequent impact on earnings and self-esteem.3 We therefore believe secukinumab should be reviewed promptly by NICE to enable timely guidance publication following marketing authorisation. 1 Boonen A, Sieper J, van der Heijde D, Dougados M, Bukowski JF, Valluri S, Vlahos B, Kotak S. The burden of non-radiographic axial spondyloarthritis. In Seminars in arthritis and rheumatism 2015 Apr 1 (Vol. 44, No. 5, pp. 556-562). 2 Baraliakos X, Braun J. Non-radiographic axial spondyloarthritis and ankylosing spondylitis: what are the similarities and differences?. RMD open. 2015 Aug 1;1(Suppl 1):e000053. 3 Martindale J, Shukla R, Goodacre J. The impact of ankylosing spondylitis/axial spondyloarthritis on work productivity. Best Practice & Research Clinical Rheumatology. 2015 Jun 1;29(3):512-23.	Comment noted. The aim of the STA process is to provide guidance close to the MA being granted.
Additional comments on the draft remit	British Society for Rheumatology	Secukinumab should be placed as an option for first line treatment of non-radiographic Axial SpA post NSAID. More studies and data on its use in anti-TNF failures in non-radiographic Axial SpA are awaited.	Comment noted.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	British Society for Rheumatology	Yes	Comment noted.
	National Ankylosing Spondylitis Society	This is accurate	Comment noted.
	Novartis	Within the first paragraph it should be clarified that radiographic axial spondyloarthritis is “also known as ankylosing spondylitis”, as specified in the ixekizumab in axial spondyloarthritis draft scope (ID1532). In the last sentence of the first paragraph a bracket should be added after “objective signs of inflammation” and before “elevated C-reactive protein”. In the final sentence of the background section; a) TA 407 should not be included as NICE guidance that recommends tumour necrosis factor-alpha inhibitors, since it recommends secukinumab, an IL-17A inhibitor. b) The final sentence should be amended to refer to NSAIDs rather than conventional therapy since this more accurately reflects TA383 and TA497 i.e. TNF-alpha inhibitors are recommended “as treatment options in people whose disease does not respond adequately to or cannot tolerate non-steroidal anti-inflammatory drugs (NSAIDs)”.	Comment noted. The background section has been amended with the suggested changes.
	UCB Pharma	UCB notes that the first paragraph of page 2, the scope mistakenly refers to TA407, in reference to tumour necrosis factor-alpha inhibitors recommended for non-radiographic axial spondyloarthritis. NICE technology appraisal guidance 383, 407 and 497 recommend tumour necrosis factor-alpha inhibitors adalimumab, certolizumab pegol, etanercept and golimumab as treatment options in people with disease that does not respond adequately to or cannot tolerate conventional therapy."	Comment noted. The background section has been amended with the suggested changes.

Section	Consultee/ Commentator	Comments [sic]	Action
		UCB would like to point out that TA407 is an appraisal of secukinumab in radiographic axial spondyloarthritis and should be deleted.	
The technology/ intervention	British Society for Rheumatology	Yes	Comment noted.
	National Ankylosing Spondylitis Society	Yes. NICE technology guidance for use of secukinumab in ankylosing spondylitis is 407 not 383 I believe.	Comment noted. The technology section has been amended with the suggested change.
	Novartis	Please specify that secukinumab is a fully human monoclonal antibody. The final sentence should refer to TA 407, not TA 383 as the NICE guidance that recommends secukinumab in radiographic axial spondyloarthritis. Importantly, TA 407 should be described as recommending secukinumab in adults whose disease has responded inadequately to conventional therapy OR TNF-alpha inhibitors (N.B. not “and”). The wording of the guidance states “Secukinumab is recommended, within its marketing authorisation, as an option for treating active ankylosing spondylitis in adults whose disease has responded inadequately to conventional therapy (non-steroidal anti-inflammatory drugs or TNF-alpha inhibitors).” Paragraphs 4.17 and 4.18 make it clear that the committee concluded that secukinumab was cost-effective both for patients that had not previously been treated with TNF-alpha inhibitors, and those had been previously treated with TNF-alpha inhibitors. We request that the section on the technology should also mention that secukinumab is both licensed and NICE recommended for patients with both plaque psoriasis and those with psoriatic arthritis (TA350 and TA445 respectively).	Comments noted. The technology section has been amended with the suggested changes. Comment noted. The technology section is designed to give information on the most relevant related technology guidance and is not designed to be exhaustive.

Section	Consultee/ Commentator	Comments [sic]	Action
Population	British Society for Rheumatology	Yes	Comment noted.
	National Ankylosing Spondylitis Society	Yes	Comment noted.
	Novartis	We consider the population is appropriately described.	Comment noted.
Comparators	British Society for Rheumatology	Yes	Comment noted. Established clinical management without biological treatments has been included for people in whom TNF inhibitors and contraindicated
	National Ankylosing Spondylitis Society	Yes	Comment noted.
	Novartis	We consider the comparators appropriate.	Comment noted.
Outcomes	British Society for Rheumatology	Yes	Comment noted.
	National Ankylosing	Yes	Comment noted.

Section	Consultee/ Commentator	Comments [sic]	Action
	Spondylitis Society		
	Novartis	We consider the outcomes specified to be broadly appropriate. However, whilst peripheral arthritis, dactylitis and extra-articular manifestations are frequently associated with nr-axSpA, they are not measured outcomes within the secukinumab phase III study (PREVENT, NCT02696031). The primary objective of PREVENT, within the EU analysis plan, is to demonstrate the superiority of secukinumab 150 mg s.c. with loading over placebo at Week 16, based on the proportion of TNF naïve patients achieving an ASAS40 response (Assessment of Spondyloarthritis International Society criteria). The ASAS instrument is a multi-domain measure capturing disease activity, physical function, pain, and patient global assessment. ASAS40 response is defined as an improvement of ≥40% and ≥2 units on a scale of 10 in at least three of the four main domains and no worsening in the remaining domain. Disease activity is further measured within the PREVENT study using the BASDAI (Bath Ankylosing Spondylitis Disease Activity Index), and ASDAS (Ankylosing Spondylitis Disease Activity Assessment) instruments. Functional capacity is measured by BASFI (Bath Ankylosing Spondylitis Functional Index). Spinal mobility is measured by BASMI (Bath Ankylosing Spondylitis Metrology Index). Disease progression is measured by sacroiliac (SI) joint oedema on MRI and by modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) on X-ray. Enthesitis is measured using MASES (Expanded Maastricht Ankylosing Spondylitis Enthesitis Score). Health-related quality of life is measured using SF-36, ASQoL, EQ-5D and FACIT-Fatigue. Overall safety and tolerability of secukinumab is also assessed.	Comments noted. The outcomes section is designed to list the most appropriate outcome measures needed for economic analysis and does not always align with what is measured in pivotal trials.
Economic analysis	British Society for Rheumatology	Yes with consideration of Biosimilars	Comment noted.

Section	Consultee/ Commentator	Comments [sic]	Action
	Novartis	The following sentence, specified within the draft scope for ixekizumab in axial spondyloarthritis (ID1532) should be included: “If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out.”	Comment noted. The economic analysis section has been with the suggested change.
Equality and Diversity	British Society for Rheumatology	Yes	Comment noted.
Other considerations	British Society for Rheumatology	No	Comment noted.
	Novartis	As per the draft scope for ixekizumab in axial spondyloarthritis (ID1532) it would also be appropriate to state that subgroups defined by prior exposure to biologics may be explored, evidence permitting.	Comment noted. The other considerations section has been with the suggested change.
Innovation	British Society for Rheumatology	No	Comment noted.
	National Ankylosing Spondylitis Society	NASS considers the technology to be innovative and could make a substantial impact on the lives of those who have not responded to or tolerated NSAIDs	Comment noted. The innovative nature of secukinumab will be considered in any appraisal of the technology.
	Novartis	Secukinumab offers a novel mechanism of action for the treatment of non-radiographic axial spondyloarthritis (nr-axSpA), targeting IL 17A and inhibiting its interaction with the IL 17 receptor. The health-related quality of life impact of nr-axSpA is similar to ankylosing spondylitis (also known as	Comment noted. The innovative nature of secukinumab will be considered in any

Section	Consultee/ Commentator	Comments [sic]	Action
		radiographic axSpA), with comparable patient self-reported disease activity and functional impairments.1 Patients with nr-axSpA are typically diagnosed in their 30's.2 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 study (PREVENT, NCT02696031) is capturing work productivity benefits via the WPAI-GH (Work Productivity and Activity Impairment - General Health). 1 Boonen A, Sieper J, van der Heijde D, Dougados M, Bukowski JF, Valluri S, Vlahos B, Kotak S. The burden of non-radiographic axial spondyloarthritis. In Seminars in arthritis and rheumatism 2015 Apr 1 (Vol. 44, No. 5, pp. 556-562). 2 Baraliakos X, Braun J. Non-radiographic axial spondyloarthritis and ankylosing spondylitis: what are the similarities and differences?. RMD open. 2015 Aug 1;1(Suppl 1):e000053.	appraisal of the technology.
Questions for consultation	National Ankylosing Spondylitis Society	NASS considers secukinumab will fit into the existing NICE pathway for spondyloarthritis after 'non-steroidal anti-inflammatory drugs' as part of 'choice of biological therapy for pain relief'.	Comment noted.
	Novartis	Have all relevant comparators for secukinumab been included in the scope? Novartis: Comparators are appropriate. Is secukinumab intended to be used in the same population that adalimumab, certolizumab pegol, etanercept and golimumab have a NICE recommendation (that is severe non-radiographic axial spondyloarthritis)? Novartis: We anticipate that secukinumab will be used in line with the recommended TNF-α inhibitors in the UK.	Comment noted. Comment noted.

Section	Consultee/ Commentator	Comments [sic]	Action
		Which treatments are considered to be established clinical practice in the NHS for: • radiographic axial spondyloarthritis • non-radiographic axial spondyloarthritis? Novartis: For radiographic axial spondyloarthritis, MQT data to December 2018 indicates that Humira dominates, with xxx patient share, followed by Benepali with xxx share. Cosentyx, Cimzia, Enbrel, Erelzi and Simponi, all have smaller patient shares. For non-radiographic axial spondyloarthritis, MQT data to December 2018 indicates that Humira dominates, with xxx patient share, followed by Benepali with xxx share, and Cimzia with xxx share. Enbrel and Simponi also have small shares.	Comments noted.
		Are the outcomes listed appropriate? Novartis: See comments above on “Outcomes”	Comment noted.
		Are the subgroups suggested in ‘other considerations appropriate? Are there any other subgroups of people in whom secukinumab is expected to be more clinically effective and cost effective or other groups that should be examined separately? Novartis: It may be relevant to explore evidence on clinical effectiveness and cost effectiveness of secukinumab in subgroups defined by prior exposure to biologics.	Comment noted.
		Where do you consider secukinumab will fit into the existing NICE pathway, ‘spondyloarthritis’?	Comment noted.

Section	Consultee/ Commentator	Comments [sic]	Action
		Novartis: We would expect secukinumab to be positioned alongside the other biologics recommended by NICE for treating severe axial spondyloarthritis. NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. Novartis: No comment. Do you consider secukinumab to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)? Novartis: Secukinumab is innovative in that it offers a novel mechanism of action for the treatment of non-radiographic axial spondyloarthritis (nr-axSpA), targeting IL 17A and inhibiting its interaction with the IL 17 receptor. Do you consider that the use of secukinumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation? Novartis: Patients with nr-axSpA are typically diagnosed in their 30's. As such, the condition impacts on both work productivity and ability to perform unpaid tasks, such as childcare.4 Effective treatment is likely to have indirect benefits in these areas that will not be included in the QALY calculation. 4 Boonen A, Brinkhuizen T, Landewé R, van der Heijde D, Severens JL. Impact of ankylosing spondylitis on sick leave, presenteeism and unpaid	Comment noted. Comment noted.

Section	Consultee/ Commentator	Comments [sic]	Action
		productivity, and estimation of the societal cost. Annals of the rheumatic diseases. 2010 Jun 1;69(6):1123-8. Do you consider that there will be any barriers to adoption of this technology into practice? Novartis: None anticipated. Secukinumab is already routinely used in UK Rheumatology centres for both Ankylosing Spondylitis and Psoriatic Arthritis. NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. • Would it be appropriate to use the cost comparison methodology for this topic? Novartis: This topic may potentially be appropriate for a cost comparison approach, and hence a Fast Track Appraisal (FTA). • Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators? Novartis: Similar or greater clinical efficacy is anticipated but cannot be confirmed until results of the PREVENT study are available. Resource use with secukinumab is anticipated to be similar or less than resource use with the TNF-α inhibitors.	Comment noted. Comment noted. Comment noted.

Section	Consultee/ Commentator	Comments [sic]	Action
		• Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant? • Novartis: The primary outcome in the PREVENT study is ASAS40. Previous models in axial spondyloarthritis have defined response based on BASDAI50 and have tracked both BASDAI and BASFI over time to determine anticipated health benefits. Whilst BASDAI and BASFI are still clinically relevant, and were measured in the PREVENT study, both ASAS and ASDAS are increasingly clinically relevant. These outcomes could in future form the basis of alternative modelling approaches in axial spondyloarthritis. • Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year? • Novartis: We are not aware of any key evidence for the comparators that are due to report within the next year.	Comment noted. Comment noted.

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

Abbvie
Merck Sharpe and Dohme
Amgen

The following consultees/commentators indicated that they endorse the comments of British Society of Rheumatology:

Royal College of Physicians