NICE National Institute for Health and Care Excellence

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Secukinumab for treating non-radiographic axial spondyloarthritis

2nd Appraisal Committee meeting

Chair presentation

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ERG: York

Chair: Jane Adam

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Company: Novartis

6th May 2021

Key issues

- Draft recommendation is for disease which has responded inadequately to TNF-α inhibitors, or people who are contraindicated or not suitable (optimised recommendation). Guidance applies to people receiving secukinumab first or second line, even though second line data is very sparse:
  - Committee accepted that secukinumab is cost effective compared with conventional care in these circumstances
  - Committee considered that secukinumab would be used when TNF-α inhibitors were unsuitable for a variety of reasons
- Company and other responders commented on:
  - Comparison with individual TNF-α inhibitors may give different cost effectiveness estimates to TNF-α inhibitors as a class
  - Use of costs of adalimumab biosimilar to represent the costs of TNF-α inhibitors
- Is the committee preference to compare secukinumab with TNF-α inhibitors as a class rather than individually fully justified?
- Is it appropriate to use adalimumab biosimilar as representative of TNF-α inhibitors costs? Will uptake in the NHS be lower than 100%?
  - If a lower uptake assumed, does this affect the committee's conclusions?

Draft recommendations in ACD

- Secukinumab is recommended as an option for treating active non-radiographic axial spondyloarthritis which has responded inadequately to non-steroidal anti-inflammatory drugs (NSAIDs), only if:
  - **the disease has responded inadequately to tumour necrosis factor (TNF)-alpha inhibitors, or these are contraindicated or not suitable**
  - the company provides secukinumab according to the commercial arrangement
- Assess response to secukinumab after 16 weeks of treatment. Continue treatment only if there is clear evidence of response, defined as:
  - a reduction in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score to 50% of the pre-treatment value or by 2 or more units and
  - a reduction in the spinal pain visual analogue scale (VAS) by 2 cm or more.

Treatment pathway

NICE guideline 65 spondylarthritis in over 16s: diagnosis and management

Non–radiographic **axSpA**

Offer physical therapy

↓

Non steroidal anti-inflammatory drugs (NSAIDS)

↓

TNF-α inhibitors
adalimumab* TA 383 (2016)
certolizumab pegol TA383
etanercept* TA383
golimumab TA497 (2018)
Stopping rule at 12 weeks
Secukinumab?

↓

Repeat with another TNF-α inhibitor (if disease has not responded, stops responding or if first TNF-α inhibitor not tolerated (TA383))
Secukinumab?

*** Since guidance, biosimilar adalimumab and etanercept are available**

At 1st committee meeting clinical experts said:

- Clinicians choose cheapest option when more than one option suitable. Currently this is adalimumab biosimilar (ACD 3.3)
- Second choice TNF-α inhibitor usually etanercept (ACD 3.3)
- Secukinumab is an option when TNF-α inhibitors are not suitable, or when the disease has not responded or stopped responding to TNF-α inhibitors (ACD 3.2)
- If a person's condition has responded to a TNF-α inhibitor they would have another, but for disease that has had an inadequate response to TNF-α inhibitors, it is preferable to try a treatment option with a different mechanism of action (ACD 3.3)

Sources of clinical evidence

comparison	source	Committee considerations
Secukinumab vs. placebo	PREVENT (RCT) Secukinumab n=185 Placebo n=184	**~90% of trial population were TNF-α inhibitor naïve** **~10% had exposure to 1 previous TNF-α inhibitor** **Primary outcome**: proportion of **TNF-α inhibitor naïve** patients achieving an ASAS40 response (disease activity) at Week 16 No data presented for people who cannot have TNF-α inhibitors, for whom conventional care is the appropriate comparator
Secukinumab vs. TNF-α inhibitors Secukinumab vs conventional care	Company network meta-analysis	**Company**: results presented vs. adalimumab, certolizumab pegol, etanercept and golimumab separately and vs TNF-α inhibitors as class* Company suggested several sources of heterogeneity between studies but data limitations made quantifying extent of effect not possible * TA383 'Committee concluded TNF-alpha inhibitors clinically effective… and, given the lack of difference in effect between them, they should be considered as a class with broadly similar, even if not completely identical, effects.'

NMA results for secukinumab compared to other treatments

[redacted]

	Outcome	BASDAI50 Response
Comparator		Odds Ratio
Adalimumab	Mean	[redacted]
	95% CrI	[redacted]
Certolizumab pegol	Mean	[redacted]
	95% CrI	[redacted]
Etanercept	Mean	[redacted]
	95% CrI	[redacted]
Golimumab	Mean	[redacted]
	95% CrI	[redacted]
TNF-α Inhibitors (Class)	Mean	[redacted]
	95% CrI	[redacted]
Conventional Care	Mean	[redacted]
	95% CrI	[redacted]

BASDAI 50 (a measure of disease activity response) was a key efficacy outcome in the model, because determined if people stopped treatment

Source: Table 11, ERG report (page 50-51)

Committee conclusions on clinical effectiveness evidence

Data	Conclusions
PREVENT	• Compared with placebo, secukinumab is effective: ASAS 40 response, BASDAI 50 response (response in disease activity) and improved function as assessed by BASFI (ACD 3.4) • Limited data from PREVENT to measure the clinical effectiveness of secukinumab when used after a TNF-α inhibitor….[But secukinumab] was likely to be clinically effective compared with placebo in this situation (ACD 3.5)
Class effect of TNF-α inhibitors	• Comparison with TNF-α inhibitors as a class appropriate
Company's network meta-analysis (described in ACD 3.8)	• '..point estimates for secukinumab were lower for some outcomes compared with TNF-α inhibitors as a class'. (including BASDAI 50 – treatment response measure used in model) • 'credible intervals around… estimates were wide … no statistically significant differences'. • 'Several sources of heterogeneity across the trials….may have affected the results … but because of a lack of data it was not possible to test whether the results were biased against secukinumab'. • Company and clinical experts did not expect a difference in clinical effectiveness secukinumab vs. TNF-α inhibitors • 'results of the company's [NMA] were uncertain … could not exclude the possibility that secukinumab may be less effective than TNF-α inhibitors

Company's cost-effectiveness model

Characteristics	Company model
Intervention	150mg of secukinumab with loading dose
Comparator	In base case analysis • conventional care (NSAIDS and physiotherapy) • TNF-α inhibitors (adalimumab, certolizumab pegol, etanercept and golimumab individually) • TNF-α combined (based on company's estimates of market share of each inhibitor)
Population	Reflected population in PREVENT. Starting cohort are TNF-α naïve

Committee conclusions on cost effectiveness

- The structure of the company's economic model was appropriate but only included the population in PREVENT:
  - ERG noted model relates only to 1st line use of secukinumab.
  - Company did not present results for people who are contraindicated for, or who cannot have TNF-α inhibitors
- Company used efficacy data for individual TNF-α inhibitor, and as a class. Committee preferred the comparison as a class
  - Company used an average of confidential market share information to cost TNF-α inhibitors as a class:
    - ERG did not consider this representative of expected 1st line use of TNF-α inhibitors in clinical practice-cheapest TNF-α inhibitor is the adalimumab biosimilar and its use in the NHS is expected to keep increasing
    - **Company**: adalimumab biosimilar is most widely used in clinical practice but inappropriate to use cost of adalimumab biosimilar for the whole class of TNF-α inhibitors because some people do not have adalimumab 1st line
    - **Committee**: costs estimated for TNF-α inhibitors for 1st-line use are likely to be closer to the cost of adalimumab biosimilar

Cost effectiveness estimates

Secukinumab has a patient access scheme:

- Secukinumab is cost effective for people who would otherwise have conventional care ICER < £20,000 per QALY gained

Because there are confidential discounts for some TNF-α inhibitors the exact ICERs were not presented in the ACD:

- Secukinumab had fewer QALYs in all company and ERG analyses.
- Committee did not consider the difference in QALYs to be minimal
- Noted in most analyses the costs of secukinumab were also higher than TNF-α inhibitors
- Committee conclusion: only recommended if **the disease has responded inadequately to tumour necrosis factor (TNF)-alpha inhibitors, or these are contraindicated or not suitable**

ICER: incremental cost effectiveness ratio

ACD consultation responses

Professional/ patient organisations	• No comments from Spondyloarthritis Special Interest Group (SIG)
Comparator company	• UCB pharma considers treatment choice should be based on appropriate choice for individual patient by clinicians-cost of lowest cost biosimilar should not be the only driver of market share calculations
Company	• No additional analyses from Novartis provided. Some minor changes requested for improved clarity.
Public (web) comments	• Query about including technology appraisal guidance into NICE guideline 65.

Stakeholder comments (UCB pharma)

Agrees with positioning of secukinumab in treatment pathway

- Agrees with clinical expert opinion in ACD (3.2) : people with no primary response or inadequate response 1st line TNF-α inhibitors should be considered for alternative rather than additional TNF-α inhibitors. DANBIO registry shows poor outcomes for repeated use of TNF-α inhibitors

Disagrees with assuming all patients in NHS will take adalimumab biosimilar 1st line

- Assumption inappropriate given heterogeneity of patient population and biases analyses in favour of TNF-α inhibitors
- Some people are contraindicated for treatment with individual TNF-α inhibitors (e.g. etanercept contraindicated if person has uveitis) and people may choose between inhibitors based on injection frequency.
- More appropriate to base on NHSE commissioning framework pricing agreement on biosimilar adalimumab
  - October 2018 to May 2019, share of adalimumab biosimilar as **1st or 2nd** line biologic across a **wide number of indications** increased to 63%. The goal of the NHSE framework was to increase this to 80%.
  - This 80% assumptions should be tested in sensitivity analyses.

Company response overview

"We agree with the draft recommendation It will give clinicians and patients freedom to choose the most appropriate treatment given each individual patient's particular circumstances"

Request wording changes to:

- Clarify statements on the cost-effectiveness of secukinumab are based on assuming costs of adalimumab biosimilar for all TNF-α inhibitors (notes secukinumab is less expensive and company considers of similar efficacy to branded golimumab and certolizumab pegol):
- State secukinumab could be considered cost-effective compared to branded TNF-α inhibitors although these are understood not to be widely used as first line biologics in UK clinical practice
- Amend statement the company model only included the population in PREVENT who had not had TNF-α inhibitors before.
  - a cost-effectiveness analysis was presented for people with prior exposure to TNF-α inhibitors (informed by a small subgroup from PREVENT) and that cost-effectiveness results for the 2nd-line population included people who had responded inadequately to TNF-α inhibitors and people who were intolerant to at least one dose of a TNF-α inhibitor.
- Other minor wording changes requested

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