NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Technology Appraisal Review Proposal paper

Review of TA340; Ustekinumab for treating active psoriatic arthritis

Original publication date:	June 2015
Review date	June 2018
Existing recommendations:	Optimised To see the complete existing recommendations and the original remit for TA340, see Appendix A.

1. Proposal

We propose that TA340 should be transferred to the 'static guidance list.'

2. Rationale

No new evidence is available that would require an update of this guidance. The guidance has been incorporated into Nice Guideline NG65 'Spondyloarthritis in over 16s: diagnosis and management'.

3. Summary of new evidence and implications for review

TA340 included evidence comparing ustekinumab to placebo. There is now evidence available comparing secukinumab and ustekinumab (Thaci et al 2015).

Has there been any change to the price of the technology(ies) since the guidance was published?
No change to list price. Under the original patient access scheme the company provided 2x45‑mg pre-filled syringes, for patients who needed the higher dose of 90‑mg, at the same total cost to the NHS as for a single 45‑mg pre-filled syringe. The patient access scheme has been withdrawn because the company now provides a 90‑mg vial at the same cost as the 45‑mg vial. TA340 was updated in March 2017 to reflect the withdrawal of the PAS.
Are there any existing or proposed changes to the marketing authorisation that would affect the existing guidance?

No
Were any uncertainties identified in the original guidance? Is there any new evidence that might address this?
The Committee considered that there is an important need for head-to-head comparisons between biological treatments for psoriatic arthritis, particularly in people for whom treatment with tumour necrosis factor (TNF) alpha inhibitors has been unsuccessful. Results of a phase IIIb randomised clinical trial comparing secukinumab and ustekinumab in people with moderate to severe plaque psoriasis have been published (Thaci et al 2015). Analysis of the results for the subgroup of patients with psoriatic arthritis (123 of 676 patients randomised) may allow a more direct comparison between secukinumab and ustekinumab. Analysis of clinical effectiveness in this subgroup has not been published, therefore there is no evidence available that would alter current guidance. Also, this trial will only partially address the clinical uncertainty identified by the committee because there is no direct evidence comparing secukinumab with biological treatments other than ustekinumab.
Are there any related pieces of NICE guidance relevant to this appraisal? If so, what implications might this have for the existing guidance?
See Appendix C for a list of related NICE guidance.
Additional comments

The search strategy from the original ERG report (for STAs) was re-run on the Cochrane Library, Medline, Medline In-Process and Embase. References from January 2013 onwards were reviewed. Additional searches of clinical trials registries and other sources were also carried out. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section above. See Appendix C for further details of ongoing and unpublished studies.

4. Equality issues

The Committee also considered whether appraising ustekinumab 45 mg alone could lead to unfair or discriminatory recommendations, if the higher dose were more effective in people weighing more than 100 kg. This is no longer relevant the company now provides a 90-mg vial at the same cost as the 45-mg vial.

When using the Psoriatic Arthritis Response Criteria (PsARC) healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect a person's responses to components of the PsARC and make any adjustments they consider appropriate.

GE paper sign off: **Helen Knight,** 24/05/2018

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Appendix A – Information from existing guidance

5. Original remit

To appraise the clinical and cost effectiveness of ustekinumab within its licensed indication for the treatment of active and progressive psoriatic arthritis

6. Current guidance

1.1 Ustekinumab is recommended as an option, alone or in combination with methotrexate, for treating active psoriatic arthritis in adults only when:

- treatment with tumour necrosis factor (TNF) alpha inhibitors is contraindicated but would otherwise be considered (as described in NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis and golimumab for the treatment of psoriatic arthritis) or
- the person has had treatment with 1 or more TNF–alpha inhibitors.

1.2 Ustekinumab treatment should be stopped if the person's psoriatic arthritis has not shown an adequate response using the Psoriatic Arthritis Response Criteria (PsARC) at 24 weeks. An adequate response is defined as an improvement in at least 2 of the 4 criteria (1 of which must be joint tenderness or swelling score), with no worsening in any of the 4 criteria. As recommended in NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis, people whose disease has a Psoriasis Area and Severity Index (PASI) 75 response but whose PsARC response does not justify continuing treatment should be assessed by a dermatologist to determine whether continuing treatment is appropriate on the basis of skin response (see NICE technology appraisal guidance on ustekinumab for the treatment of adults with moderate to severe psoriasis).

1.3 When using the Psoriatic Arthritis Response Criteria (PsARC) healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect a person's responses to components of the PsARC and make any adjustments they consider appropriate.

1.4 People whose treatment with ustekinumab is not recommended in this NICE guidance, but was started within the NHS before this guidance was published, should be able to continue ustekinumab until they and their NHS clinician consider it appropriate to stop.

7. Research recommendations from original guidance

The Committee considered that there is an important need for head-to-head comparisons between biological treatments for psoriatic arthritis, particularly in people for whom treatment with tumour necrosis factor (TNF) alpha inhibitors has been unsuccessful.

8. Cost information from original guidance

The list price for ustekinumab is £2147 per 45‑mg vial (excluding VAT; British national formulary online [accessed February 2015]). The recommended dose of ustekinumab is an initial dose of 45 mg, followed by a dose 4 weeks later and further doses every 12 weeks thereafter. A dose of 90 mg may be used in people with a body weight over 100 kg.

Appendix B – Explanation of options

When considering whether to review one of its Technology Appraisals NICE must select one of the options in the table below:

Options	Consequence	Selected – 'Yes/No'
A review of the guidance should be planned into the appraisal work programme. The review will be conducted through the Technology Appraisals process.	A review of the appraisal will be planned into the NICE's work programme.	No
The decision to review the guidance should be deferred to a specific date or trial.	NICE will reconsider whether a review is necessary at the specified date.	No
A review of the guidance should be combined with a review of a related technology appraisal. The review will be conducted through the MTA process.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the specified related technology.	No
A review of the guidance should be combined with a new technology appraisal that has recently been referred to NICE. The review will be conducted through the MTA process.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the newly referred technology.	No
The guidance should be incorporated into an on-going clinical guideline.	The on-going guideline will include the recommendations of the technology appraisal. The technology appraisal will remain extant alongside the guideline. Normally it will also be recommended that the technology appraisal guidance is moved to the static list until such time as the clinical guideline is considered for review. This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal.	No

Appendix B

Options	Consequence	Selected – 'Yes/No'
The guidance should be updated in an on-going clinical guideline[1].	Responsibility for the updating the technology appraisal passes to the NICE Clinical Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn. Note that this option does not preserve the funding direction associated with a positive recommendation in a NICE Technology Appraisal. However, if the recommendations are unchanged from the technology appraisal, the technology appraisal can be left in place (effectively the same as incorporation).	No
The guidance should be transferred to the 'static guidance list'.	The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider. Literature searches are carried out every 5 years to check whether any of the Appraisals on the static list should be flagged for review.	Yes
The guidance should be withdrawn	The guidance is no longer relevant and an update of the existing recommendations would not add value to the NHS. The guidance will be stood down and any funding direction associated with a positive recommendation will not be preserved.	No

[1] Information on the criteria for NICE allowing a technology appraisal in an ongoing clinical guideline can be found in section 6.20 of the guide to the processes of technology appraisal.

Appendix C – other relevant information

1. Relevant Institute work

Published

NICE technology appraisal guidance 433 (February 2012) Apremilast for treating active psoriatic arthritis

NICE technology appraisal guidance 433 (May 2017) Certolizumab pegol and secukinumab for treating active psoriatic arthritis after inadequate response to DMARDs

NICE technology appraisal guidance 199 (August 2010) Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis. Reviewed August 2016 where a decision was made to move it to the static list

NICE technology appraisal guidance 220 (April 2011) Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis. Reviewed August 2016 where a decision was made to move it to the static listIn progress

NICE technology appraisal guidance in development [GID-TA10173] Abatacept for treating active psoriatic arthritis after DMARDs [ID993] Expected publication date: July 2018

NICE technology appraisal guidance in development [GID-TA10278] Ixekizumab for treating active psoriatic arthritis after DMARDs [ID1194] [ID993] Expected publication date: October 2018

NICE technology appraisal guidance in development [[GID-TA10237] Tofacitinib for treating active psoriatic arthritis after DMARDs [ID1220] [ID993] Expected publication date: December 2018

NICE guideline NG65 (February 2017) Spondyloarthritis in over 16s: diagnosis and management

NICE pathway Spondyloarthritis. Last updated: January 2018

2. Details of new products

Drug (company)	Details (phase of development, expected launch date)	In topic selection
Risankizumab (AbbVie)	Phase 3	[redacted]
Upadacitinib (AbbVie)	Phase 3	[redacted]
Brodalumab (Valeant/Amgen)	2 phase 3 studies for psoriatic arthritis; one completed in 2015, results not available via clinicaltrials.gov; one terminated in 2015 results available	[redacted]

3. Details of changes to the indications of the technology

Indication and price considered in original appraisal	Proposed indication (for this appraisal) and current price
The original indication is unchanged: "Ustekinumab has a marketing authorisation in the UK for use alone or in combination with methotrexate 'for the treatment of active psoriatic arthritis in adult patients when the response to previous non biological disease modifying antirheumatic drug (DMARD) therapy has been inadequate'"	The manufacturer has indicated that: "[redacted]

4. Registered and unpublished trials

Trial name and registration number	Details
Impact of Concomitant Methotrexate on Efficacy, Safety and Adherence of Ustekinumab-treatment in Patients With Active Psoriasis Arthritis (NCT03148860)	Methotrexate (MTX) co-medication can improve the therapeutic effect of biological therapies (e.g. TNF-inhibitors) in rheumatoid arthritis (RA), but its role in Psoriatic Arthritis (PsA) remains unclear. Differences in phenotypical manifestations between PsA and RA might influence the impact of co-medication, treatment response and treatment adherence differently. Independent from this data, the impact of use of MTX in Ustekinumab (UST) treated patients with active PsA remains unclear: No data from Randomized Clinical Trials (RCTs) are available to address the questions whether add-on of MTX to UST monotherapy, or the other way around. Study Type: Interventional (Clinical Trial) Allocation: Randomized 198 participants Study Completion Date: December 31, 2019 Recruiting

5. Relevant services covered by NHS England specialised commissioning

Nothing relevant

Appendix D – References

Thaci, D (2015) Secukinumab is superior to ustekinumab in clearing skin of subjects with moderate to severe plaque psoriasis: CLEAR, a randomized controlled trial Journal of the American Academy of Dermatology 73 (3) 400-409 https://doi.org/10.1016/j.jaad.2015.05.013