

Appendix G - professional organisation statement template

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Ustekinumab for treating active and progressive psoriatic arthritis

Thank you for agreeing to give us a statement on your organisation's view of the technology and the way it should be used in the NHS.

Healthcare professionals can provide a unique perspective on the technology within the context of current clinical practice which is not typically available from the published literature.

To help you in making your statement, we have provided a template. The questions are there as prompts to guide you. It is not essential that you answer all of them.

Please do not exceed the 8-page limit.

About you

Your name: *Nick Levell MD FRCP MBA on behalf of the Therapy & Guidelines sub-committee*

Name of your organisation: *BRITISH ASSOCIATION OF DERMATOLOGISTS*

Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology? **Yes**
- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)? **Yes**
- an employee of a healthcare professional organisation that represents clinicians treating the condition for which NICE is considering the technology? **Yes**
- If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc)? **Member of Therapy & Guidelines sub-committee of the British Association of Dermatologists**

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What is the expected place of the technology in current practice?

How is the condition currently treated in the NHS? Is there significant geographical variation in current practice? Are there differences of opinion between professionals as to what current practice should be? What are the current alternatives (if any) to the technology, and what are their respective advantages and disadvantages?

Currently psoriatic arthritis is diagnosed and treated by consultant rheumatologists working in secondary and tertiary care. Most patients also have psoriasis or a family history of psoriasis, so are co-treated by consultant dermatologists in secondary/tertiary care.

This means that patients often require treatment for both aspects of psoriatic disease.

When standard systemic oral drugs are ineffective, biological therapies against TNF- α are used. Anti-TNF- α therapies are recommended by NICE for both psoriasis and psoriatic arthritis. Ustekinumab does have NICE approval to treat psoriasis but not yet for joint disease.

Data from the PSUMMIT1 trial (McInnes et al., 2013) suggest that psoriatic arthritis may benefit from ustekinumab, particularly if there is enthesitis, dactylitis and axial involvement.

There are no head-to-head studies for anti-TNF- α agents vs. ustekinumab in the treatment of psoriatic arthritis and it is not known if ustekinumab prevents radiological deterioration in psoriatic arthritis.

It is useful to have an alternative therapy to treat individuals with moderately severe psoriasis and psoriatic arthritis if there is a contraindication to or primary or secondary failure of anti-TNF- α therapies.

McInnes IB, Kavanaugh A, Gottlieb AB, et al, on behalf of the PSUMMIT 1 Study Group. Efficacy and safety of ustekinumab in patients with active psoriatic arthritis: 1 year results of the phase 3, multicentre, double-blind, placebo-controlled PSUMMIT 1 trial. Lancet 2013; published online June 13. [http://dx.doi.org/10.1016/S0140-6736\(13\)60594-2](http://dx.doi.org/10.1016/S0140-6736(13)60594-2).

Are there any subgroups of patients with the condition who have a different prognosis from the typical patient? Are there differences in the capacity of different subgroups to benefit from or to be put at risk by the technology?

- (i) Individuals would benefit in whom anti-TNF- α therapy is contraindicated including those with established heart failure or an ejection fraction of <50%***
- (ii) Those with a history of demyelination***
- (iii) Possibly from PSUMMIT1 trial those patients with dactylitis, enthesitis and axial involvement and severe psoriasis rather than those with polyarticular and oligoarticular PsA***

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In PSUMMIT 1 (McInnes et al, 2013) there were three major adverse cardiovascular events on ustekinumab – myocardial infarction at 8 weeks and 22 weeks, and stroke at 29 weeks. A possible link between major adverse cardiovascular events and interleukin 12/23 blockers, especially in the first 12 weeks of treatment, is debated in dermatology (Ryan et al, 2011). Data from safety registries are awaited to determine whether this risk is real. In clinical practice expert advice (Dr Ruth Murphy) suggests it does not seem to be the case.

Ryan C, Leonardi CL, Krueger JC, et al. Association between biologic therapies for chronic plaque psoriasis and cardiovascular events: a meta-analysis of randomized controlled trials. JAMA 2011; 306: 864–71.

In what setting should/could the technology be used – for example, primary or secondary care, specialist clinics? Would there be any requirements for additional professional input (for example, community care, specialist nursing, other healthcare professionals)?

Secondary and tertiary Consultant Rheumatologists would initiate treatment for joint disease. Many patients would be under shared care with Consultant Dermatologists if they also had psoriasis. Ongoing care would be by both teams, but the lead being taken by one or other team depending on whether joint disease, or skin disease was the predominant problem.

Many patients are managed by specialist rheumatology or dermatology nurses, depending usually attached to secondary care support the use of the drug in individuals stabilised on therapy.

There is a requirement for long-term safety monitoring and patients should be entered onto the skin ([BADBIR](#)) or rheumatological long-term safety monitoring registries. This may requires input by research nurses.

If the technology is already available, is there variation in how it is being used in the NHS? Is it always used within its licensed indications? If not, under what circumstances does this occur?

Ustekinumab is prescribed by dermatologists for patients with moderately severe psoriasis for which there are NICE guidelines. If these individuals also have psoriatic arthritis then there is variation in practice between those doctors who would consider ustekinumab. The PSUMMIT1 trial data have supported its use but it does not yet have NICE guidance for use in psoriatic arthritis.

Please tell us about any relevant **clinical guidelines** and comment on the appropriateness of the methodology used in developing the guideline and the specific evidence that underpinned the various recommendations.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

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The British Association of Dermatologists, a NICE-accredited guidelines producer, has clinical guidelines for the use of [biological therapies in the treatment of moderate to severe psoriasis](#). Ustekinumab is included as an option for the treatment of moderately severe psoriasis.

The advantages and disadvantages of the technology

NICE is particularly interested in your views on how the technology, when it becomes available, will compare with current alternatives used in the UK. Will the technology be easier or more difficult to use, and are there any practical implications (for example, concomitant treatments, other additional clinical requirements, patient acceptability/ease of use or the need for additional tests) surrounding its future use?

If appropriate, please give your view on the nature of any rules, informal or formal, for starting and stopping the use of the technology; this might include any requirements for additional testing to identify appropriate subgroups for treatment or to assess response and the potential for discontinuation.

Since ustekinumab is given at three monthly intervals it is useful for individuals who find weekly or fortnightly injections a problem. Since it is subcutaneous in its administration rather than intravenously then this is an additional benefit over infliximab (an anti-TNF).

This is particularly useful for children, those with compliance difficulties and those in prison.

The drug will only be routinely prescribed following NICE approval and even then, if not prescribed as first-line, may be challenged by commissioning groups. The sequential use of biological therapies, whilst supported in the NICE psoriasis guidelines (CG153) is sometimes challenged, creating postcode variation in practice.

As it is not yet possible to target those individuals most likely to benefit from ustekinumab, it is likely to be prescribed sequentially following failure, side effects or non-response to anti-TNF- α agents.

Ustekinumab should be used before anti-TNF- α agents in individuals with heart failure or demyelination. It may also be used first in groups that particularly benefit from the three monthly injections.

If you are familiar with the evidence base for the technology, please comment on whether the use of the technology under clinical trial conditions reflects that observed in clinical practice. Do the circumstances in which the trials were conducted reflect current UK practice, and if not, how could the results be extrapolated to a UK setting? What, in your view, are the most important outcomes, and were they measured in the trials? If surrogate measures of outcome were used, do they adequately predict long-term outcomes?

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

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What is the relative significance of any side effects or adverse reactions? In what ways do these affect the management of the condition and the patient's quality of life? Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently during routine clinical practice?

The entry criteria for PSUMMIT1 included those with psoriatic arthritis who had failed to respond to 12 weeks' therapy with a non-steroidal anti-inflammatory drug, DMARD or failure with an anti-TNF- α . Therefore some individuals were entered who might have responded to an anti-TNF- α agent.

We do not yet know which patients with psoriasis and psoriatic arthritis are most likely to benefit from ustekinumab. A head-to-head study of ustekinumab vs. an anti-TNF- α drug would establish relative efficacy in psoriatic arthritis, and assess whether ustekinumab can achieve equivalent improvements for the radiological effects in psoriatic arthritis.

One report suggested that individuals commenced on ustekinumab were at a higher risk of having a myocardial infarction during the first 12 weeks of treatment. In clinical practice this not observed and does not generally influence its prescription. Safety data from national registries such as [BADBIR](#) is required.

PSUMMIT1 reported significant improvement of standard ($p < 0.001$) quality of life measures for HAQ-DI and DLQI.

Any additional sources of evidence

Can you provide information about any relevant evidence that might not be found by a technology-focused systematic review of the available trial evidence? This could be information on recent and informal unpublished evidence, or information from registries and other nationally coordinated clinical audits. Any such information must include sufficient detail to allow a judgement to be made as to the quality of the evidence and to allow potential sources of bias to be determined.

None added

Implementation issues

The NHS is required by the Department of Health and the Welsh Assembly Government to provide funding and resources for medicines and treatments that have been recommended by NICE technology appraisal guidance. This provision has to be made within 3 months from the date of publication of the guidance.

If the technology is unlikely to be available in sufficient quantity, or the staff and facilities to fulfil the general nature of the guidance cannot be put in place within 3 months, NICE may advise the Department of Health and the Welsh Assembly Government to vary this direction.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

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Please note that NICE cannot suggest such a variation on the basis of budgetary constraints alone.

How would possible NICE guidance on this technology affect the delivery of care for patients with this condition? Would NHS staff need extra education and training? Would any additional resources be required (for example, facilities or equipment)?

Consultant Dermatologists and Rheumatologists familiar with biological therapies, their indication, monitoring and use would not need any additional education or training to deliver ustekinumab for psoriatic arthritis as the drug is now used routinely in psoriasis. Nurse specialists will often support and monitor the use of biological therapies for affected patients. Research nurses and medical researchers will maintain safety data in registries.

Equality

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 this appraisal:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which [the treatment(s)] is/are/will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could lead to recommendations that have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

There should be equity of access for use of these agents across England and Wales. Rules concerning sequential prescribing on biological drugs should be clear to avoid variation between postcodes.