Professional organisation statement template

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: [redacted]

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? √
- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)?
- an employee of a healthcare professional organisation that represents clinicians treating the condition for which NICE is considering the technology? If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc.)?
- other? (please specify)

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

How is the condition currently treated in the NHS?

Psoriasis affects 2% of the population but only a small proportion of therapy-resistant cases, or cases with multiple pathologies that contra-indicate other therapies ever need biological interventions.

Is there significant geographical variation in current practice?

The majority of Dermatology Departments are prescribing biological therapies but there is inconsistency with the rate of uptake which may be more to do with support facilities, employment of biologic nurses and possibly restraints on drug budgets.

Are there differences of opinion between professionals as to what current practice should be?

There is good agreement on the type of patient who should be considered for biologic therapy. However, the evidence is not strong to favour a particular ordering of therapy

What are the current alternatives (if any) to the technology, and what are their respective advantages and disadvantages?

Etanercept, efalizumab, infliximab and adalimumab. The advantage of etanercept is a longer track record of safety but disadvantages are that treatment does usually need to be continuous and some (larger) patients require 50mg twice weekly which is not currently approved by NICE. Efalizumab has an advantage of being licensed for continuous therapy and having a novel mode of action. Preliminary data suggest there may be genetic predictors of response. Disadvantages are flu-like side effects, possible exacerbation of psoriatic arthritis and more brittle control with the possibility for exacerbation or rebound of psoriasis. Infliximab is currently the most effective agent but has to be given by infusion and under monitoring having the potential for allergic reactions, infusion reactions and loss of efficacy through antibody formation. Adalimumab is similar to infliximab but has convenience of once fortnightly dosing. Adalimumab and Infliximab seem to carry the highest risk of reactivation of latent tuberculosis.

Are there any subgroups of patients with the condition who have a different prognosis from the typical patient?

Patients who develop psoriatic arthritis have worse outcomes as do those with co-morbidities such as depression, obesity, cardio-vascular disease or harmful lifestyles eg smoking/alcohol.

Are there differences in the capacity of different subgroups to benefit from or to be put at risk by the technology?

One would prefer to offer a drug active in arthritis to those with concomitant psoriatic arthritis. There is less long term safety data with Ustekinumab but short-term large-scale trials have not shown any unexpected harms or significant rate of adverse events compared to other biological interventions for psoriasis.

In what setting should/could the technology be used – for example, primary or secondary care, specialist clinics?

Should be used in secondary care, prescribed only by dermatologists experienced in immunotherapy and treating severe psoriasis.

Would there be any requirements for additional professional input (for example, community care, specialist nursing, other healthcare professionals)?

Yes, support may be required by biologics nurses and community services such as Healthcare at Home for advice, monitoring and instruction in administration of therapy. However, unlike the other biologic drugs it is only given every three months. Thus you could argue that the patient should attend the dermatologist and receive the subcut injection in the clinic without the need for community services. (Would help with compliance as well)

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?

This does not currently apply although licensing of this agent is considered to be fairly imminent and this might change. It is unlikely to be used out-with the labelled indication.

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.

Ustekinumab will be included in the next updated version of the British Association of Dermatologists guidelines for the use of biological interventions in psoriasis due in 2009 and based on the same pivotal trials that will be likely to be presented to NICE by the manufacturer..

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?

There are no direct head-to-head comparative data but the headline response rates to Ustekinumab are somewhat better at 12 weeks than adalimumab and fall slightly short of those with infliximab with 67% and 72% of patients achieving PASI 75 by week 12 for the 45mg and 90mg doses respectively. Maximal efficacy is evident between week 20 and week 24. Disease responses are maintained with continued therapy for up to 1.5 years. Increasing the dose from 45mg to 90mg is associated with better results and increasing the dose increases the likelihood of response but not in all patients.

The remarkable property of this treatment is that it can be administered every 12 weeks to maintain improvement. This is not pharmacokinetic but appears to be related to a remittive action. Median time to relapse being 15 weeks, longer than for other biologicals. This offers convenience for administration and should, depending on how pricing is fixed, reduce some of the drug costs. It has been suggested that the pricing will take into account different dosing needs of patients and will not penalise patients requiring a higher dose (i.e. the costs will be the same regardless of the dose). This is a novel approach to drug dosing and is very welcome. The trials show that intensification of treatment with more frequent 8 weekly therapy or increasing the dose will be necessary in some patients especially where the target of therapy is to clear or almost clear the patient's psoriasis. Partial response was more likely in those with prior inadequate response to biologic therapy.

In summary, Ustekinumab has a unique mode of action, a very long biological half-life and very good efficacy including moderate activity against psoriatic arthritis. Therefore it should be positioned on a par with etanercept and adalimumab. It is also likely to be useful in situations where there is failure to or contraindication to the use of anti-TNF agents. However, to date only about 2000 patients have received the drug in trials so safety is difficult to evaluate and, given the long biological half-life, predicting how to respond to adverse events will be difficult.

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.

BAD guidelines for biologics assess response at around 12 to 16 weeks and recommend discontinuation if response criteria are not being met. These are PASI 75 or greater or PASI 50 with a 5 point improvement in DLQI. Data from different drugs are given at different time points so there is not consistency across agents in the timing of the assessment of response.

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?

All of the normal response criteria have been applied and the population in the trials captures on average more severe disease, mean PASI of 20. Fewer patients have had prior systemic agents (about 55%). Nevertheless the trials are robust and of sufficient duration with sufficient subgroup analysis to suggest that external validity will be high.

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?

Overall, rates of adverse events were similar to placebo, and there was no consistent evidence for a relationship between dose or frequency of dosing, and the occurrence of adverse events. These were as would be expected from a biological therapy including upper respiratory tract infection, nasopharyngitis, arthralgia, cough, and headache.

Injection site reactions were uncommon (1.5%), perhaps because of the infrequency of drug administration. Antibodies (neutralizing) develop in approximately 5% of patients and are associated with poorer responses to therapy. The incidence of serious infections was 0.4 to 0.8% in the different subgroups and similar to the placebo phase. There were 3 incident cases of non cutaneous cancers and 4 cutaneous cancers in one study and 7 cutaneous cancers and one other (non cutaneous) cancer on therapy, with similar rates in the placebo arm.
No cases of tuberculosis, demyelination or lymphoma were identified. Numbers are small but it would be expected that specific side effects of the anti TNF class of biologics would be avoided in patients using this therapy. However, it may have its own unique problems of infection as Th-17 cells are targeted and have functional importance in response to infection.

Given the relative lack of long term safety data, the BAD strongly feel that registration and long term follow up via the BAD Biologics Intervention Register (BADBIR) be recommended for all patients receiving this technology, if approved.

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.

The company may have other trial data not yet in the public domain and in other indications including a paper by Sandborn in Gastroenterology on Crohn's disease.

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.

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)?

Screening for latent tuberculosis would be advised for patients starting therapy and this requires support with tuberculin skin testing and, where appropriate, interferon assays which are subject to another HTA appraisal and have cost implications. Staff currently providing care for patients on biological therapies will not need additional training other than an understanding of the profile of the technology.