

**Healthcare professional group/clinical specialist statement**

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: Dr A.D. Ormerod**

**Name of your organisation (if applicable): 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) Chair of Therapy Audit and Guidelines committee  
British Association of Dermatologists

**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?

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?

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)?

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?

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.

*The BAD produced evidence based guidelines for the use of biologicals in psoriasis with a rigorous methodology. These clearly define the context in which licensed biologicals should be used in the UK including disease severity and other criteria for eligibility. These criteria were accepted by NICE in TA 103. Unlike the NICE appraisal the BAD guideline did systematically review the literature available at the time (Before July 2005) for Infliximab. The guidelines do state that infliximab is not licensed for psoriasis which is obviously no longer the case. Since publication there has been one major long term phase 3 study published and another is expected shortly.*

*Currently severe psoriasis is managed by consultant dermatologists in secondary care with a range of potentially toxic interventions none of which are entirely satisfactory for long term management of what is often a lifelong disease. These require considerable expertise in appropriate choice and monitoring. These include phototherapy with or without systemic psoralens, methotrexate, ciclosporin and acitretin. Only when these treatments fail or are contra-indicated is a patient currently considered for biological interventions. Because of the history of Infliximab being available for other diseases it was the first biological to be used in many centres as on “off label” therapy for severe and difficult psoriasis. It will continue to be indicated for these difficult unresponsive or severely affected patients with other pathology and should only be administered in specialised surroundings of secondary care where staff are trained, infusion facilities exist*

### 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.

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?

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?

#### Advantages

*Three randomised, placebo-controlled trials have been conducted in patients with moderate to severe, stable chronic plaque psoriasis. (Reich et al 2005, Chaudhury et al 2001 Gottlieb et al 2004). All trials demonstrated infliximab therapy to be highly effective at inducing disease remission. The onset of improvement occurs within the first 2 to 4 weeks of treatment and reaches maximum benefit by week 10 in the majority. 87% of patients receiving a standard induction course of therapy (5mg/kg at weeks 0, 2 and 6) achieved PASI 75. Time to relapse following successful 'induction' therapy is highly variable between individuals, and may depend on the initial dose given: 73% of those given 10mg/kg during induction maintained at least a 50% improvement in PASI scores at week 26 compared to 40% of those given 5mg/kg. The largest study of 378 patients treated for 12 months confirmed a marked efficacy with 80% of patients achieving PASI 75 and 57% achieving PASI 90 at 10 weeks. Efficacy was preserved by 2 monthly maintenance infusion of 5mg / kg in the majority of patients, 61% maintaining PASI 75 and 45% maintaining PASI 90. These patients also manifested dramatic improvements in dermatology specific and general quality of life scores (Reich et al 2006)*

*Several case series indicate infliximab monotherapy to be of benefit in patients previously resistant to multiple systemic therapies and there are a number of case reports documenting efficacy in severe unstable psoriasis and generalised pustular psoriasis. Clinical experience within the guideline group further supports the value of infliximab in these clinical circumstances. (Smith et al 2005).*

*Advantages of Infliximab are clearly its marked efficacy and speed of improvement. Although not assessed formally in head to head clinical trials the studies are consistently showing better results than found with other licensed biologicals including etanercept and efalizumab. BAD guidelines recommendations are that*

*Infliximab is useful in clinical circumstances requiring rapid disease control for example, in unstable erythrodermic or pustular psoriasis, due to its very rapid onset of action and high response rate. Normally Infliximab is given as monotherapy for psoriasis but where a patient is requiring combination therapy combination with methotrexate has been widely assessed in rheumatoid arthritis and can be recommended. There is also limited data on combinations with other immunosuppressives. In those patients who respond to therapy, regular maintenance infusions may avoid the risk of loss of efficacy seen in some patients receiving intermittent as required repeat infusions on disease relapse.*

*Chaudhari U, Romano P, Mulcahy LD et al. Efficacy and safety of infliximab monotherapy for plaque-type psoriasis: a randomised trial. Lancet 2001;35; 1842-7*

*Gottlieb AB, Evans R, Li S et al. Infliximab induction therapy for patients with severe plaque-type psoriasis: A randomized, double-blind, placebo-controlled trial. J Am Acad Dermatol 2004;51: 534-42.*

*Reich K, Nestle FO, Papp K, Ortonne JP, Wu Y, Bala M, Evans R, Guzzo C, Li S, Dooley LT, Griffiths CE. Improvement in quality of life with infliximab induction and maintenance therapy in patients with moderate-to-severe psoriasis: a randomized controlled trial., Br J Dermatol. 2006 Jun;154(6):1161-8.*

*Reich K, Nestle FO, Papp K, Ortonne JP, Evans R, Guzzo C, Li S, Dooley LT, Griffiths CE; EXPRESS study investigators  
Infliximab induction and maintenance therapy for moderate-to-severe psoriasis: a phase III, multicentre, double-blind trial. Lancet. 2005 Oct 15-21;366(9494):1367-74*

*Smith CH, Anstey AV, Barker JN, Burden AD, Chalmers RJ, Chandler D, Finlay AY, Griffiths CE, Jackson K, McHugh NJ, McKenna KE, Reynolds NJ, Ormerod AD  
British Association of Dermatologists guidelines for use of biological interventions in psoriasis 2005. Br J Dermatol. 2005 Sep;153(3):486-97.*

#### *Disadvantages*

*In general, infliximab and etanercept are well tolerated . However, infections and malignancy are a significant clinical concern although the actual associated risks are unknown, particularly in psoriasis. Previous or concomitant immunosuppressant treatment and PUVA therapy may compound such risks. Additional, serious potential toxicities include demyelinating disease and heart failure. Infusion reactions occurring during or within 1-2 hours of treatment affect up to 20% of all patients treated and rarely may rarely result in anaphylactic shock. Antibodies to infliximab may develop during therapy, these may have implications for reduced efficacy and increasing the risk of allergic reactions but the relationship is imprecise. Serious and opportunistic infections are also associated with Infliximab. Tuberculosis is a risk particularly associated with infliximab. Heart failure may be exacerbated by Infliximab although Clinical trial data in psoriasis show no excess risk of heart failure although selection bias*

*The important question of whether infliximab is responsible for an increased incidence of malignancy is not adequately resolved despite much investigation. Regulatory authorities have encouraged transparency in the SPC meriting special warnings. Whether the risk is theoretical or real patient selection is merited to avoid*

*Infliximab in patients at higher risk of malignancy and increased vigilance for those on therapy. In patients treated for psoriasis prior phototherapy and skin cancer risks may be very important here.*

*Infliximab has also been associated with immunological reactions including anti-nuclear antibodies and lupus - like syndromes, hepatitis and demyelination*

#### **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.

#### **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)?