From: Reetan Patel
Sent: 25 September 2007 23:04
To: Natalie Bemrose
Subject: FW: Adalimumab in psoriasis

Attachments: Adalimumab statement mst.doc

From: [redacted] [mailto:[redacted]]
Sent: 25 September 2007 21:45
To: Reetan Patel
Cc: [redacted]
Subject: Adalimumab in psoriasis

Dear Reetan, Attached is a copy of the submission from the British Association of Dermatologists. Essentially as there have been no new publications this has not changed from that we submitted last November.
Regards, [redacted],
[redacted]

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: [redacted]

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 and biologics subgroup with a wide range of expertise and input to these appraisals.

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 majority of patients with psoriatic arthritis will by definition have psoriasis. The psoriasis may be mild, moderate or severe. Accepting that this technology appraisal is primarily for psoriatic arthritis we would like the patient's skin disease to be considered as an important additional factor. Where the skin disease is severe or disabling patients are likely to have benefits not only for their joints but also for their skin and to have a greater benefit from treatment in the cost / benefit analysis.

The BAD produced evidence based guidelines for the use of biologicals in psoriasis with a rigorous methodology (Smith et al). 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. However, Adalimumab has not yet been included in these guidelines as we await publication of relevant clinical trials and licensing for this indication.

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
In terms of efficacy for cutaneous psoriasis the phase 2 trial of 147 patients showed an improvement of PASI score of more than 75% (PASI 75) in 80% patients treated weekly and 53% in patients treated every other week; and were clear or almost clear in 76 and 49% respectively. At week 48 of an open label follow up 52% and 44% respectively were clear or almost clear. (Gordon et al 2006). Although comparative trials have not been performed these results are as good as the most effective licensed therapy (infliximab) and are better than those found with etanercept or efalizumab). Post hoc analysis shows PASI-75 to be achieved in 74% (weekly dose) and 69% (fortnightly dose) of patients fulfilling the BAD guidelines criteria for initiating a biological therapy (Gordon et al 2005). This confirms the results to be generalisable to UK clinical practice. These patients also showed marked improvement in quality of life with reductions of 15.5 and 14.6 in DLQI. (a worthwhile improvement being 5 points on this scale). Post hoc analysis also shows that patients with or without associated psoriatic arthritis respond similarly (Menter et al). A good proportion of patients maintain long-term responsiveness with 67% of patients treated fortnightly and 73% of those on weekly treatment maintaining PASI 75 over 60 weeks of therapy. Adalimumab also provides a useful alternative when patients have failed to respond to, or become refractory to other anti TNFalpha treatments such as infliximab.

As a fully human anti-TNF alpha agent adalimumab has advantages over other currently available agents inconvenience as it is administered subcutaneously; acceptable results following bi-weekly administration; and also greatly reduced risk of immunological reactions be these anaphylactic, vasculitic, neutralising antibodies or induction of auto-antibodies.

In a paper presented at the European Academy of Dermato-venereology in October 2006 Saurat reported on a trial of 271 patients in which Adalimumab was compared to methotrexate. With adalimumab in standard doses (80mg initial then 40 mg alternate weeks) 80% achieved PASI 75 (n=110) at 16 weeks compared to only 35.5% with methotrexate (dose not stated in my source documents) (n=110). More detail is required and should become available but this appears to be the first head to head study showing an advantage of biologic therapy over conventional therapy.

Disadvantages
Exposure in person years in other indications is less than that with existing anti-TNF alpha agents.

Gordon KB, et al. Clinical response to adalimumab treatment in patients with moderate to severe psoriasis: double-blind, randomized controlled trial and open-label extension study. J Am Acad Dermatol. 2006 Oct;55:598-606

*Gordon et al. Efficacy and safety of adalimumab in the treatment of chronic plaque psoriasis in patients who meet some of the criteria for biologic interventions in accordance with British Association of Dermatologists Guidelines. Br. J. Dermatol 2006, **155** suppl 1. Page 32 abs P-28*

*Menter MA et al Adalimumab efficacy and safety results in patients with moderate to severe chronic plaque psoriasis with and without psoriatic arthritis. J. Am. Acad. Dermatol **2005;53**: 2713.*

Smith CH, Anstey AV, Barker JNWN, Burden AD, Chalmers RJG, Chandler D, Finlay AY, Griffiths CEM, 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 ;153:486-97.

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

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)?

Facilities in dermatology are developing for delivery and monitoring of other biologics but are by no means fully established. Delivery of adalimumab for Psoriatic arthritis would be within the rheumatology service but where patients with significant skin disease are being treated we feel there should be collaboration with consultant dermatologists. It may be appropriate for some patients with more severe skin disease to be registered in the British Association of Dermatologists Biologics Register where the long term safety and efficacy of adalimumab for the patient's skin disease can be more reliably determined in the real world as opposed to clinical trials.