

Appendix G - professional organisation submission template

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Adalimumab for treating moderate to severe hidradenitis suppurativa [ID812]

Thank you for agreeing to make a submission 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 submission, 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: Drs John Ingram* and Nemesha Desai, and the British Association of Dermatologists Therapy and Guidelines sub-committee**

Name of your organisation: British Association of Dermatologists (BAD)

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? If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc)? No
- other? (please specify)

* = JI:

First author of the Cochrane review "Interventions for hidradenitis suppurativa"

** = ND:

Chief Investigator multicentre observational study UK Hidradenitis Suppurativa, plus

- i. Clinical lead for tertiary UK Hidradenitis service at St. John's Institute of Dermatology; Guy's & St. Thomas' NHS Trust
- ii. NHS England Subspecialty lead Hidradentis Suppurativa
- iii. Member of European Hidradenitis Suppurativa Foundation

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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?

In the NHS a stepwise approach to treatment is taken, based on disease severity. The medical treatment ladder commences with topical antimicrobial therapy, such as clindamycin 1% solution, for mild disease. The next step is single agent oral antibiotics, most commonly the oral tetracycline group and then combination antibiotic treatment with clindamycin 300mg twice daily and rifampicin twice daily for 10-12 weeks, for moderate disease. For moderate to severe disease unresponsive to these therapies a number of options may be considered, including acitretin for males and non-fertile females, dapsone or other immunomodulators such as ciclosporin. Metformin may be a helpful adjunct. For severe disease unresponsive to other therapy, biologic anti-TNF treatments are considered, including infliximab and adalimumab.

Surgical management is utilised as stand-alone intervention or in combination with medical therapy and include extensive excision of an involved region when only one, or a few regions are involved. Limited surgical procedures include deroofing of sinus tracts and narrow margin excision; however, both are associated with a high rate of recurrence at the surgical margins. In other European countries, STEEP (Skin Tissue Sparing Excision with Electrosurgical Peeling) is performed more often for moderate disease, but is again associated with a high rate of recurrence.

There is a reasonable degree of consensus between UK clinicians regarding the medical treatment pathway, in line with the European guidelines, as demonstrated in a recent UK survey of current practice (Ingram et al 2015). However, there was less consensus regarding the timing of any surgery and the type of surgical procedure. The survey did not highlight any particular geographical variation, although access to plastic surgery expertise may have affected the timing and type of surgery.

The main alternative to adalimumab, in terms of medical therapy, is infliximab. Infliximab has the advantage of being dosed by weight, which is particularly important in the context that many hidradenitis suppurativa (HS) patients are overweight or obese and has potential for rapid onset of action. However, the IV mode of administration makes infliximab less convenient for patients compared to the subcutaneous dosing of adalimumab which can be administered in the patient's own home.

Cost is a very important issue. Based on the RCT evidence available, which is summarised in the recently-published Cochrane review (Ingram et al 2015), adalimumab is only effective when given at a dose of 40 mg weekly. This represents

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twice the standard dose used for psoriasis and other conditions and, at current prices, will make adalimumab cost nearly twice as much as infliximab.

Long term safety data is currently lacking regarding administration of adalimumab at twice the standard psoriasis dose. However, trials up to 12 months in duration have not raised significant concerns regarding infection rates or other adverse effects, compared with infliximab or the standard dose of adalimumab.

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?

This is essentially unknown due to a lack of cohort and registry studies.

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)?

Adalimumab should be instigated and monitored in secondary care, ideally via specialist HS and/or biologic clinics. This will ensure appropriate patient selection and monitoring. However, some centres may not have dedicated clinics currently. Once established on treatment, administration of adalimumab can take place in the patient's own home.

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?

Current variation in the use of adalimumab mainly relates to local funding issues. Prior to adalimumab obtaining its European licence for HS, funding was sought on an individual patient basis.

*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.*

Dr Ingram is currently leading the British Association of Dermatologists UK guideline development group for HS, using GRADE methodology, and the guidelines will take about another 12 months to be finalised. European Dermatology Forum guidelines were published earlier this year (Zouboulis et al 2015). The guidelines are evidence-based but the quality of evidence was not formally assessed and the final treatment algorithm is based on a consensus approach.

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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?

Prior to use of anti-TNF therapy for HS, there were no other equivalent medical treatment options for severe, widespread HS. Oral immunomodulators were used with limited success and surgery was the other option, depending on the number of regions involved.

As discussed above, the main alternative biologic to adalimumab is infliximab. Infliximab has the advantage of being dosed by weight and being cheaper than adalimumab weekly therapy. However the evidence base for infliximab in HS is weaker, it is unlicensed for HS, and the IV route of administration is less convenient for patients. In addition, the single RCT investigating infliximab for HS reported primary outcomes after 8 weeks and so we do not know whether infliximab's efficacy is sustained for this chronic condition.

Safety monitoring for biologic therapy in HS is similar to the framework currently used for psoriasis. However, as discussed above, safety data for adalimumab weekly dosing is currently relatively limited.

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?

Using current trial evidence and based on its European licence, adalimumab should be considered for moderate to severe HS unresponsive to standard therapy. The definition of standard therapy may need further discussion, particularly because adalimumab is currently the only systemic therapy licensed for HS in the UK. Standard therapy could be defined as topical therapy, oral tetracyclines, and the clindamycin and rifampicin combination. Acitretin for males and infertile females could also be considered, but this therapy is unlicensed and based on case series evidence only. Surgery may also need to be considered, particularly when disease is localised to only one or two sites.

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The rules for starting and stopping adalimumab should be based on both physician and patient reported outcome measures. There is only limited validation data for outcome measures in HS. Hurley staging is a useful physician-reported baseline measure and moderate to severe disease corresponds to Hurley stages 2-3. The Hurley system is unresponsive to change and so HiSCR (Kimball et al 2014), based on a count of the number of inflammatory lesions, could be used in which a 50% reduction in baseline score represents treatment success. The physician's global assessment (PGA) is an alternative measure that is quicker to perform.

The two standard patient reported outcomes in HS are quality of life and pain. In the adalimumab trials, quality of life was measured using the Dermatology Life Quality Index (DLQI). A DLQI score of 11 or more represents a severe impact on quality of life, while the mean score of patients entering the largest HS adalimumab trial (Kimball 2012) was approximately 15. The minimal clinically important difference for the DLQI scale is 4 points (Basra et al 2015), which could be used as one of the stopping rules. Pain can be measured on a visual analogue scale (VAS) and a 50% reduction in baseline pain is usually considered an adequate response.

The primary outcome in Kimball et al 2012 was measured at 16 weeks and this is an appropriate duration of treatment to assess disease response after commencing adalimumab.

There is no data regarding differential responses in particular subgroups of HS patients. The trial conditions probably do reflect in general how adalimumab would be used in UK clinical practice, however real-life experience is limited because adalimumab has only recently gained its HS licence and approval for its use in HS has been on a named patient basis in severe cases where all other therapies have failed.

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 clinical trials and clinical practice have not demonstrated adverse effects that differ from use of adalimumab in psoriasis and other inflammatory conditions. The main issue is that there is only limited data regarding the long term safety profile of weekly adalimumab therapy.

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.

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The Cochrane review of “Interventions for hidradenitis suppurativa” has just been published in October 2015 (Ingram et al).

Implementation issues

The NHS is required by the Department of Health 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 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)?

Adalimumab therapy for HS is likely to mirror the systems already in place for psoriasis, including dermatology biologic clinics and biologic specialist nurses in secondary care. An expansion of this service may be required however. Delivery systems to transport adalimumab to the patient’s home are already in place for psoriasis and other inflammatory conditions.

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.

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No particular equality issues identified.