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National Institute for Health and Clinical Excellence

**Use of tumour necrosis factor alpha (TNF a) inhibitors (adalimumab, and infliximab [review]) for Crohn's disease**

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Royal College of Nursing

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**Introduction**

With a membership of over 400,000 registered nurses, midwives, health visitors, nursing students, health care assistants and nurse cadets, the Royal College of Nursing (RCN) is the voice of nursing across the UK and the largest professional union of nursing staff in the world. RCN members work in a variety of hospital and community settings in the NHS and the independent sector. The RCN promotes patient and nursing interests on a wide range of issues by working closely with the Government, the UK parliaments and other national and European political institutions, trade unions, professional bodies and voluntary organisations.

**Appraisal Consultation Document – RCN Response**

The Royal College of Nursing welcomes the opportunity to review the Appraisal Consultation Document (ACD) of the technology appraisal of Use of tumour necrosis factor alpha (TNF a) inhibitors (adalimumab, and infliximab [review]) for Crohn's disease. The RCN was asked to comment on:

- **Whether we consider that all the relevant evidence has been taken into account**
- **Whether we consider that the summaries of the clinical effectiveness and cost effectiveness are reasonable interpretations of the evidence and the preliminary views on the resource impact and implications for the NHS are appropriate**
- **Whether we consider that the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS.**

- **Whether we consider that there are any equality related issues which need special consideration and which are not covered in the ACD?**

The Appraisal Consultation Document was reviewed by nurses working in the Gastroenterology and Stoma Care area of health. The collective response to this ACD was developed on behalf of the RCN Gastro and Stoma Nursing Forum, a professional network within the Royal College of Nursing for nurses working in and those who have special interest in this area.

### **Point 1.1**

The document should also reflect the European consensus '*All currently available anti TNF therapies appear to have similar efficacy and adverse event profiles, so the choice depends on availability, route of delivery, patient preference, costs and national guidance*' (ECCO L5, RG D)

In our experience, many patients have to go on to weekly rather than standard 2 weekly Humira even when induction regime of 160/80mg is used which would significantly affect the over all cost of treatment. This is an important issue if adalimumab is being recommended as being more cost effective than infliximab. Equally many of our patients are able to increase the interval between infliximab treatments to as long as four months, in some cases certainly three months rather than every eight weeks add infliximab which again will affect the cost in favour of infliximab.

There is very little evidence base and no head to head studies that show Adalimumab is more effective than Infliximab as first line biologic. Both anti TNFs are equally as efficacious. The choice regarding which preparation to use first-line cannot be made on the basis of cost only, which seems to be the case in this document. This negates the aspect of evidence based patient and physician choice in the selection of anti TNF therapy. Indeed some patients do not benefit from home administration and those with needle phobia do not wish to take responsibility for the decision to inject, therefore, where there is an alternative treatment, patient choice and tolerance should be considered. The evidence for these statements is still only in

abstract form but the message is clear: *home administration is not for every patient.*  
(Kemp K et al (2009; Allen et al (2008).

Some patients benefit from regular review when coming for their infusions, either because their condition warrants it or because they prefer the medical model. Also some may be non-compliant with monitoring or administration which makes safety an even bigger issue.

**Point 1.2 –**

It would be helpful to state the age which is defined as the end of adolescence for this guidance.

There is clear evidence of patients that are primary non-responders to infliximab and secondary non-responders to infliximab who then go on and have a very good response to adalimumab. To date we do not have the information that patients who fail to respond or lose response to adalimumab will go on to have the same response to infliximab. However this is common practice in Rheumatology and one would expect patients with Crohn's Disease to behave similarly, as yet we do not have the evidence base for this approach to treatment.

**Pont 1.3**

We feel that it is an excellent point to reassess the disease after 12 months of treatment as currently there is no evidence base for exit strategies however we would have concerns about stopping Anti TNF  $\alpha$ . It would be sensible to reassess the patient through imaging and/ or endoscopy to assess for mucosal healing while also using CDAI or Harvey Bradshaw to assess for remission in line with ECCO guidelines. Discussing the discontinuation of treatment with the patient is essential once investigation has confirmed clinical and endoscopic remission. There would have to be a low threshold for recommencement of treatment to prevent the situation where a patient has further severe exacerbation before treatment is restarted.

Obviously, if the medication is effective then disease should be inactive and therefore there will be evidence of mucosal healing. If the patient does not relapse and a sustained remission is achieved then continued use would surely be a waste for both the patient, taking medication that is unnecessary with possible long term effects we are as yet unaware of and waste of NHS resources.

This is obviously very debateable and needs to be considered in greater depth. We would consider 12 months a reasonable review period only if it is in conjunction with and it includes a concise and clear treatment and assessment pathway which is responsive to clinical/endoscopic findings. This treatment strategy should be discussed with the patient at the start including what is possible to achieve, what is not and what remains unclear and an agreement for exit strategy at the end of 12 months with plan for alternative maintenance. This is particularly pertinent to paediatric patients who inevitably (hopefully!) have many years to live with the possible long-term consequences of treatment and one assumes would always have an excuse not to stop so as to enable them get through life choices for example GCSEs, A levels, university and other stressful life events!

The current guidance can be open to different clinical interpretation leading to potential disparity in service provision/delivery nationwide.

We also have to reflect upon NICE guidance in dermatology/ rheumatology who are not subjected to such restraints in their clinical decision making. We would have hoped for parity through the specialties.

We would like further clarification on this point but accept readily that re-evaluation of the patient is vital and exit strategy must be addressed in this document.

#### **Point 4.3.4**

We are pleased to see that the issue of fistulising perianal disease has now been addressed and this will mean that many trusts should be able to treat this group of

patients without having to request exceptional funding, an issue that has all too often stood in the way of timely treatment.

The rest of the ACD does not seem to really be able to differentiate anything other than the cost between the technologies. We all know of course that the choice of preparation is far more complex and that this, patient choice and suitability for the different preparations should be a major guiding factor.

**Equality related issues which need special consideration and which are not covered in the ACD**

We are not aware of any specific need/special consideration with respect to this technology at this stage. We would however, ask that any guidance issued should show that equality issues were considered and that the guidance demonstrates an understanding of issues concerning the patients' age, faith, race, gender, disability, cultural and sexuality where appropriate.

**References**

Kemp K et al (2009) 'Patient perception of home biologic therapy adalimumab' J Crohns Colitis, Vol 3 Issue 1, S82

Allen et al (2008) 'How do patients with inflammatory bowel disease want to have their biologic administered?' UEGW, P0709