

**Comments received from a cross-section of NACC Medical Advisers which illustrate their view of the consequences of not approving maintenance use of antiTNF therapy.**

**Summary of key issues**

- Maintenance with antiTNF therapy is already used sparingly and focused on patients who do not have alternatives.
- Many doctors already have a programme of review after a certain period.
- The improvement for patients' quality of life given by maintenance treatment is very significant and will be much reduced by an episodic treatment approach.
- There are significant drawbacks in terms of service delivery, NHS costs and patients' convenience from a Relapse and Re-treat approach.
- Professional opinion is very much against this aspect of the guidance.

**Dr M**

This is potentially disastrous! Although my numbers are small i.e. about 5 patients currently on maintenance and with my colleagues perhaps 15-20 in all for our population of 550,000 they have been very carefully selected and face an absolute nightmare if they have to give up their medication. One patient will certainly lose her colon and have to have an ileostomy at age 40, another lad will be back to horrible anal fistulae, recurrent perianal sepsis requiring surgery etc and another young woman who already has an ileostomy would go back to chronic ill health and unemployment having been well enough on adalimumab to go back to work etc.

I cannot believe that NICE has turned to experts in the field who don't recognise what a dramatic difference these drugs make to a small minority of patients who would otherwise cost a small fortune in surgical procedures, admissions, steroid side effects etc. Episodic treatment would just result in deterioration in function, surgical loss of bowel and with ability for patients to self administer we'd be back to the problems with getting day cases in for infusion etc.

**Dr B**

I probably have no more than a dozen on maintenance therapy, mainly with Humira rather than Infliximab. I don't really plan to keep them on lifelong therapy but would like the opportunity to maintain treatment for 12-18 months

I find it very useful for patients who are entering a critical phase of their life, the most obvious being teenagers and adolescents entering final year at school/college. There are also others for whom a further flare up or surgery would be hugely inconvenient - I have a patient on maintenance therapy whose husband is terminally ill and for whom she is the main carer.

As I would take most patients off maintenance therapy at some point, I suspect I would not have any more than twenty patients on maintenance at any one time. In my experience, about 50% of patients who respond to anti TNF relapse after stopping.

In terms of comments to NICE, I can't understand why they seem to be flying in the face of all the evidence and asking the Gastroenterologists in UK to do something so out of step with all the other developed countries.

#### **Dr M**

I have about 6-8 people on regular Infliximab and three on adalimumab. I have two that I'd like to start now and one is likely to be induction only, but the other to be maintenance as well. I think the annual figure will be small - only 3-4 per year

The idea of managing these patients by letting them relapse is appalling for them: it screws up employment opportunities and it makes them have to expect to get ill before anything can be done. For most people with more than mild IBD, best management is to give them stable good health not to leave them on a see-saw. Also, we suspect that this episodic therapy may make therapy less effective long term so this seems intrinsically a bad idea.

Episodic rather than regular therapy would mean unplanned work - extra urgent appointments in full clinics, trying to find somewhere for the treatment to be administered and, almost certainly, more admissions. Those with dominant pain often end up getting admitted when they relapse because of the pain. For those with severe disease I don't usually try to stop Infliximab if it has worked. They have usually already tried and failed other second line agents. I think we should be trying to keep people in employment and out of hospital. This is a retrograde decision that will increase suffering.

#### **Dr T**

We have 37 patients on infliximab and 19 on adalimumab. In our population (80% secondary care, 20% tertiary referral, 1200 under active follow up with CD) I would expect 30 new patients/year who have had recurrent episodes of severe CD and demonstrably failed maximal maintenance therapy

The effect of a switch to episodic therapy for patients would be a major reduction in quality of life; increased hospitalisation (at least 1 episode/year for each such patient); reduced working capacity with danger of job loss; increased use of steroids with adverse impact on bone density; increased surgery, for some of whom this would mean colectomy and permanent stoma.

If we have to operate an episodic rather than a maintenance regime it would remove an important therapeutic option and put back the management clock by 10 years. As one of the leading centres for CD care in Europe, colleagues outside the UK are already simply astonished that scheduled therapy for such patients is not already an option.

NICE should allow scheduled re-treatment before relapse in those who have had recurrent episodes of severe CD that has needed and responded to anti-TNF therapy and demonstrably failed maximal maintenance therapy

## Dr P

We have approx 5% of our Crohn's patients on regular anti-TNF therapy (most people estimate 5-10%) – we probably start another 15 per year (and probably stop almost as many for various reasons); provoking relapse by stopping seems grossly unfair on the patients and is undoubtedly damaging (at least for a proportion) for their prospects of responding to future treatments and increased likelihood of provoking reactions. Of course Adalimumab has never been trialled for 'as and when' usage so it is perverse that this option should be recommended.

For the patients in whom we use anti-TNF the likelihood of relapse depends on whether they already on immunosuppressant treatment or not: for those already on (i.e. in whom immunosuppressives are not working) the likelihood of relapse is VERY high unless anti-TNF is maintained (say 80%); for the others where anti-TNF is given and e.g. azathioprine started at the same time (takes 3-4 months to work) there is a better chance that the aza will kick in and hold remission (say 50-60% likelihood of this 'bridge' to immunosuppressive treatment working – i.e. ~40% might end up relapsing without regular anti-TNF).

## Dr C

I have about 20 pts on maintenance IFX although have used it in more, stopped because of loss of efficacy or other reasons. We don't have an accurate data base for me to give you the precise figure. I have three pts on maintenance adalimumab. I would anticipate *considering* maintenance in 12 - 20 pts per year although of course some of these would not respond so would not go on with them. There is no doubt some will relapse on maintenance and develop loss of efficacy - I guess 30 - 40 % eventually but in those who don't the improvement in their QoL is enormous.

it would be devastating for patients to have to switch to episodic when the maintenance regime is keeping them so well and it is not so easy to organise episodic treatment - often there are no beds on Programmed Investigation Units for 2 or 3 weeks so pts would potentially suffer that time waiting for their treatment. The beauty of maintenance is that they can plan ahead knowing their dates and knowing they will remain well.

NICE should know that patients and Consultants are right behind NACC in objecting to the proposed guidelines. It is important that we use these drugs wisely and effectively, but the patients whose lives have been transformed should not be betrayed,

## Dr S

We have 26 patients with Crohn's on maintenance biologicals, about half on Infliximab and half on Adalimumab (our population is 250 000 with over representation of young adults). We start about 5 new patients on maintenance a year all starting on Infliximab and moving to Adalimumab when secondary failure or reactions occur.

We only use maintenance in patients if they have relapsed despite full dose immunomodulators, or if unable to tolerate it. We review their ongoing need for maintenance regularly and take the opportunity to stop whenever possible. Of those we have stopped leaving on immunomodulators alone, about half have relapsed and

required steroids and going back on maintenance, with re-induction. The ones that relapsed did so about 3 months after stopping, for one patient this meant a severe attack whilst heavily pregnant, which required admission and steroids.

#### **Dr R**

We currently have about 15 on maintenance infliximab & 5 on Adalimumab, with approximately 5 per new patients/year starting. Changing to episodic treatment will have very significant effects on our patients as they will begin to feel unwell, lose time from work, cease social activity etc every few weeks which is a nonsense. In addition the NHS struggles to do things at short notice so there would be potential for further delays between the patient complaining of recurrent symptoms and their next infusion.

There would need to be a major re-think in the way we run the service as we work across site so patients would have to attend one hospital to be assessed & sent across town for the infusion. Regular infusions can be scheduled & other services can be planned.

From our experience I would guess that at least 50-60% of patients would require repeated re-induction each year. NICE need to look carefully at their calculations, particularly the cost of repeated admissions & recurrent surgery which will be inevitable if this goes ahead. In addition the devastating and immeasurable effect of a stoma on the life of a young patient with Crohn's.

#### **Dr M**

We have about 40 patients on infliximab and 8 on adalimumab. We would consider treatment in 12 – 20 patients a year. The infliximab patients have a range of treatments including maintenance and on flare up treatment.

The main advantage of maintenance is that patients can be kept well rather than repeatedly flaring up and being ill prior to treatment. This is especially important in fistulating disease where the NICE guidance would be total madness. You could not wait for patients to refistulate and then say we will start treatment again.

For some patients all they need is a couple of doses and maintenance treatment is not needed, but if they do relapse at say 12 weeks I can see no advantage to waiting until they have relapsed before treating. It's a question of whether you are using the treatment to keep them well or just trying to patch them up when they get ill.

I don't think the cost of not using anti tnf treatment has been calculated reliably. I do support a register of patients on anti tnf treatment and I do think we need research into an exit strategy for anti tnf treatment.

#### **Dr P**

We currently have about 10 patients on maintenance infliximab - 5 have been on maintenance for longer than a year. I suspect we are rather conservative with our use of IFX and it is growing. In terms of switching to episodic treatment I think that this would be unrealistic for at least 3 of our 10 as one has just had her dosing interval shortened to 6 weeks and another 2 are just about managing to make it through 8 weeks.

If we went to episodic treatment then booking would be a logistical nightmare as we have to fit into relatively few slots in the endoscopy department. I am shocked this is being blocked. How can you invoke cost effectiveness when the alternative is an operation and removal of ones bowel not to mention the risk of further surgery.

**Dr M**

We have approximately 30 infliximab patients and 5 Adalimumab, and consider treatment with antTNF in about 20 each year. Loss of maintenance treatment would in many cases lead to loss of employment and social problems. Episodic treatment would only be okay if they can have treatment at an early stage of relapse and not have to wait until they get significantly unwell. My guess is that the average time to relapse after induction would be around once every 6 months.

It would be reasonable middle ground to allow one significant relapse after induction therapy but then administer further treatment with the use of another marker such as calprotectin, crp or symptoms depending upon the pattern of disease that the patient has i.e. some patients do not have early CRP rise but do have early symptom warning signs. The solution is to find an early indicator of relapse which should keep all parties happy.

**Dr S**

We have about 120 patients in the county out of 600,000 population, split between Infliximab and adalimumab 110:10. My guess is that we would see 25 new patients each year. If these patients had to switch to episodic treatment, relapsing before being retreated, it would lead to comparative chaos. The anticipated relapse rate in 1<sup>st</sup> year would be 30-40% e.g. 40+ patients who would all need re-assessment prior to re-treatment. Some would fail to respond, some would react to therapy etc. We would need more space in our rapid response clinic and would struggle with the job planning of the nurse who gives our infusions. At the moment she schedules things to accommodate the 120 patients and fits around their work and education commitments e.g. late afternoon appointments, half term appointments etc. This would not be feasible and we would have to go back to a re-active service.

*In addition we received detailed comments from Professor Rampton and Dr Hamlin which I understand have been submitted through the website consultation.*

Richard Driscoll  
NACC  
October 2008

Dr C – paediatric

We currently have 12 paediatric patients on regular/maintenance infliximab  
We have one child who has just started on adalimumab. We would probably want to start maintenance infliximab on about 3-4 patients each year

When initially learning how to use infliximab we tried to administer it on an as needed basis. We found that they relapsed frequently and that it was more difficult to induce remission. Furthermore we have observed that symptoms suggestive of relapse frequently commence about 7-8 weeks after an infusion and so they need their next infusion at about this time. There is also a subset of patients in whom time, following infusion, to onset of symptoms suggestive of relapse gets progressively shorter such that they need more frequent infusions. It is important to remember that these are patients who have had a very difficult time achieving and maintaining remission and in whom we are facing only limited opportunity to optimise growth and pubertal progression. Stopping and starting infliximab would compromise these goals.

We have also noted a remarkable improvement in quality of life in almost all patients on maintenance treatments. Without the use of maintenance therapy we would compromise the quality of life, growth and pubertal progression for all those patients who are successfully maintained on infliximab. I would like to stress the importance we attach to the role of infliximab in optimising growth, pubertal progression, quality of life and prevention of progression to surgery in those under 16 years of age.