crohn's and colitis UK
Inform Support Research

Ulcerative colitis (moderate, severe) – infliximab (review TA140) adalimumab (review TA262) & golimumab (2nd line) [ID695]

NICE Appraisal Consultation Document, October 2014

Crohn's and Colitis UK response

Summary

- There is a clear and defined need for biological drugs to be available to people with moderate to severe Ulcerative Colitis, for whom conventional treatments have failed, using stopping rules which would bring this in line with the guidance for Crohn's Disease (TA187)
- Neither surgery or conventional treatment are appropriate comparators for biological drugs as conventional treatment has, by definition, failed and, unless by patient choice, surgery should be considered a last resort when all appropriate medical options have been explored
- Considerable uncertainties arise from the assumptions on which the modelling is based in terms of:
    - lack of representativeness of the patient population being considered
    - extrapolation of short-term data to a lifetime horizon
    - lack of stopping rules
    - full costs, complications and risks of surgery
    - small sample on which health utility values are based
    - selection of conventional therapy as a comparator, when this has already failed this group of patients
- There are significant equality/diversity issues in terms of effectively compelling patients in this group to elective or potential emergency surgery, in particular for young people who have not begun a family and whose fertility may be affected, and for religious groups such as Muslims, for whom this may impact on religious practices and cause particular distress.

About Crohn's and Colitis UK

Crohn's and Colitis UK is the major UK charity offering information and support to anyone in the UK affected by these conditions, which come under the umbrella description Inflammatory Bowel Disease or IBD. Established in 1979, the charity's services include information and support services, a wide range of accredited information sheets and booklets, and a nationwide network of locally-based groups. The charity, which currently has 28,000 members UK-wide, also raises awareness, campaigns for improved health and public service provision for patients, and funds vital research.

Introduction

We welcome the opportunity to comment on the Appraisal Consultation Document. We are extremely disappointed with the preliminary recommendation that the three biological treatments under review are not considered to be an effective use of NHS resources for

those who have moderate to severe Ulcerative Colitis (UC) and for whom conventional treatments have failed. We believe that this has been based on invalid assumptions. If upheld, this decision is likely to leave this group of patients with no effective medical treatment options, very low quality of life, increased fear and anxiety over disease progression, increased potential for surgery and increased risk of complications and cancer. Patients will be aware of the option of biological therapy and their inability to access this which will lead to further anxiety and distress. Additionally, this is likely to have significant implications for the NHS, in particular in terms of admissions to hospital.

Our comments are informed by valuable illustrative feedback from individuals with Ulcerative Colitis, which has been included throughout. A separate document collating more than 50 individual submissions to this review has been produced and will be forwarded alongside this response. The points raised below are based on published research, expert consensus statements and guidelines and advice from experienced clinicians.

We have sought to address the following areas identified as being of interest to the Appraisal Committee

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the provisional recommendations sound and a suitable basis for guidance to the NHS?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?

1. Has all of the relevant evidence been taken into account?

It is our view that significant evidence has not been fully taken into account in relation to the costs, complications and impact of surgery, identified treatment pathways, quality of life, implications of uncontrolled disease, patient population, and projections of usage over time. This is explored further below.

i) Surgery

We welcome the Committee's agreement that surgery is not a relevant comparator for most patients with moderately to severely active disease. While it can offer the individual concerned the feeling they have 'got their life back', for many it is not an option that they want to consider except as a last resort when all available options have been exhausted, and can bring with it a range of potential complications, which may require further treatment and ongoing management. There can also be an associated profound psychological and social impact, for example, in terms of body image and self-esteem. For those who are facing this at an age when they have just begun to form relationships and do not yet have a family, this can be especially difficult.

There is documented evidence that increased use of biologics in IBD has led to a reduction in colectomy rates, which we would suggest is a highly desirable outcome in terms of patient care. From 2005-2011, following the approval and increasing use of anti-TNF therapy, the total colectomy incidence rate has decreased by 16.1% every year to 0.9 per 100 ulcerative colitis patients.[1]

It has been posited that 'colectomy is not a cure for the disease but rather the substitution of a large problem with smaller problems, including faecal incontinence, pouchitis, irritable

pouch syndrome, cuffitis, anastomotic ulcer and stenosis, missed or de-novo Crohn's disease and, in young females, reduced fecundity.[ii]

The national clinical audit of inpatient care for adults with ulcerative colitis documents 32% of UC inpatients experiencing post-surgical complications in elective surgery and 35% in non-elective surgery.[iii]

Guidelines for the management of inflammatory bowel disease in adults[iv] state that 'Clinical outcomes after pouch surgery are variable'. Drawing on evidence from the Pouch Registry, they highlight the following factors:

- Fecundity (fertility) in women is reduced by 40%-50%
- Nocturnal seepage (of faeces) is 8% after one year, rising to 15.4% at 20 years (other studies have suggested this may be as high as 32%)
- Median frequency of defecation is five per 24 hours, once at night (some studies have put this higher)
- Up to 50% of patients who undergo ileal pouch surgery for ulcerative colitis suffer from pouchitis (inflammation of an ileo-anal pouch) – reported risk factors include younger age at colectomy and extensive Ulcerative Colitis
- There is an increased risk of thromboembolic events

These considerations, in addition to potential impotence for men and risk of pouch failure, will have a significant impact on quality of life and play a large and understandable part in preferences for medical treatment options over surgery. For example, Cohen et al[v] found that medical management of refractory UC was associated with a better ability to sleep, better stool consistency and fewer daytime and night-time trips to the toilet than the surgical patients. Berndtsson and Oresland[vi] found the quality of life of patients undergoing pouch surgery for UC had not changed one year after surgery compared with that before surgery.

The ongoing need for stoma care and the psychological and social impact of body image and self-esteem are also key factors. People have told us:

"Surgery would have been a massive emotional and psychological barrier for our son at this stage in his life."

"Surgery was on the cards, but my mum, dad and I begged the surgeon not to do it."

"Personally I'm not prepared for the drastic surgery of having my colon removed."

There are numerous additional costs related to surgery which have been highlighted by other stakeholders, especially the British Society of Gastroenterology, and which we do not believe have been fully taken into account. These include:

- Potential second or third operations (e.g. restorative protocolectomy with ileoanal pouch is usually undertaken as two operations; colectomy with ileostomy may be followed by pouch surgery at a later date or permanent ileostomy)
- Ongoing stoma care and appliances (estimated at £5,000 per year by Clinical Commissioning Groups for up to 50 years for younger patients)
- Potential fertility treatment for young women after surgery
- Hospital costs for the treatment of infections and other complications
- Psychological support – IBD-related surgery or hospitalisation is associated with a significant risk for depression and anxiety.[vii]

While there may still be a necessity for surgery for some patients at a later date, following treatment with a biological drug, it should not be assumed that this is inevitable or that individuals will remain on biological therapies throughout their lives. Stopping rules that would have significant effect on the modelling and cost-effectiveness are covered in vi) below.

ii) Ongoing conventional treatment for this population

As the scope of this review applies specifically to those for whom conventional treatment has failed, the use of this in the modelling is not appropriate. People with UC have told us:

"I have had 3 years of constant flare ups and no remission. I have been hospitalised numerous times and been on every type of medication from a range of enemas, mercaptopurine, azathioprine and numerous others – none worked."

"Despite corticosteroids, azathioprine and other drugs, nothing was working. The steroids caused him great distress and made him very difficult company. Trying to work was a nightmare and he experienced crushing fatigue."

"Since I received my diagnosis in 2007, I have been on several kinds of mesalazine, azathioprine (I reacted badly to it), mercaptopurine, methotrexate, regular extended courses of prednisolone. When none of this worked effectively, my anaemia became so bad I was hospitalised and had to have a blood transfusion of 2 units of blood along with fluids and steroids."

iii) No/inadequate treatment: chronic active disease

Therefore, the only valid comparator in this case, as defined by the scope of the review, 'Infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy' is no treatment or inadequate treatment and the implications that these 'options' bring for quality of life, potential emergency surgery, hospitalisation, and complications, including cancer risk. This is explored further below in terms of the key factors that need to be adequately reflected in the modelling or any subsequent interpretation of the results.

a) Quality of life impact of chronic active Ulcerative Colitis

IBD substantially impairs patients' health-related quality of life.[viii] [ix] Factors that impact on quality of life include disease course, prescribed treatments, psychosocial factors and socioeconomic effects.[x] [xi] Disease course includes severity and extent of disease and frequency of relapses, which have a direct impact on the symptoms experienced by patients with Ulcerative Colitis, including abdominal pain, diarrhoea, rectal bleeding, weight loss, nausea, vomiting and extraintestinal features such as fatigue, arthritis or ocular symptoms.

Prescribed treatments for Ulcerative Colitis influence these symptoms as a result of their efficacy and side effects. Disease course and prescribed treatments affect the physical and psychosocial function of children and adults with Ulcerative Colitis and, by consequence, their quality of life.

Social function can be impaired with inability to work, attend school, participate in leisure activities, or have intimate relationships. Research shows that young people aged 16-25 with IBD who have not yet entered full-time employment often feel that their condition has compromised their education and significantly limited their career aspirations. There is a clear associated "productivity loss" by health state, whereby the lowest score for health state (Visual Analogue Score 0-2.5) corresponds with a 71% productivity loss[xii]

Emotional function is affected by difficulty in coping with personal lives and feelings of anger, embarrassment, frustration, sadness, and fears of needing surgery or developing cancer.[xiii] Anxiety and depressive illness is higher in people with IBD[xiv], with mood disorders at least in part a consequence of the IBD itself[xv] and its medical treatment (such as corticosteroid therapy and surgery, specifically colectomy and stoma formation). Additionally, most reports indicate that stress may be involved in triggering relapse.

"My 'moon face' from the constant use of prednisolone was depressing and because of my ill health my hair became really thin. Prednisolone also affected my mood. I was so angry and unhappy. This also kept me awake at night, so I took sleeping pills.

The isolation I have felt has been overwhelming. I can't take my children to the park, for a walk or play date or any of the other simple things that I used to take for granted. I do not have any kind of social life myself as it is simply not possible for me to go out when I may need to open my bowels with no warning. My relationship with my husband is also under a lot of pressure for obvious reasons. I am 35 years old and feel like an old woman. Instead of being in the prime of my life, my world has become so small due to this horrific disease and so have the lives of my children. The constant tiredness and the mood swings caused by all the steroids I take have made me a pretty poor mum. Recently my 2 year old son had to have an operation and I was too ill to stay with him in hospital overnight. It broke my heart. I want to get a job, enjoy my children and just start living again."

Patients with active and quiescent IBD often report symptoms of fatigue. Studies have demonstrated that fatigue measurement scores in patients with IBD are comparable to scores reported in cancer patients.[xvi]

"I was diagnosed in December 2009 with UC and became poorly very quickly. During this time my quality of life changed dramatically. I found it difficult to hold down my full time job and by the time the weekend came I was so exhausted from visits to the loo, from working and at times having accidents that I could not leave the house and at times I couldn't even manage to get out of bed. I would go as far to say that I have absolutely no life at all. This condition had a huge impact on my family too, I couldn't go on holiday or days out with them and they were so worried."

"During the majority of my time living with UC and the ever-changing drugs, I had no quality of life. I was off sick from work for 8 months. I was unable to drive my children to or from school or make them their breakfast as this was the time, usually until about midday, that I could not leave the toilet. There was no fun time with my 3 wonderful children or my husband, I was always in bed, in pain or on the toilet. We did not cuddle or play, because if any of them touched my tummy, it would be so sore. This period of illness really affected my confidence. My friends gave up coming around as I was so poorly. My quality of work really dropped. I continuously made mistakes because of the side effects from all the drugs."

b) Complications of chronic active disease:

Both osteoporosis and vitamin D deficiency are common in IBD. The major risk factors for osteoporosis complicating IBD are age, steroid use and disease activity.[xvii]

Anaemia is a common complication of IBD. Iron deficiency and anaemia of chronic disease are the commonest causes of anaemia in IBD. Drug-induced anaemia secondary to azathioprine, mercaptopurine or sulfasalazine also occurs.[xviii]

"When I am unwell the constant anaemia make everyday life feel like wading through treacle, the pain can be crippling. The very real concern of faecal incontinence gives me physical symptoms of stress as well as affecting me emotionally and mentally."

"He was struggling to maintain a healthy weight, was constantly feeling sick, rushing to the toilet and in pain and missing a great deal of his work at a stage in this career that was very important to him. He was unable to continue his sport and his social life was negligible. He had to take medication to digest his food."

"Just before I got admitted again and started on the infliximab, my mum had to try to get me out of the house to just walk up the road and back. I didn't make it half way without having an accident and I ran home and was in the bathroom as my mum helped me get tidied up. And I actually had hit rock bottom and I said to my mum then I just want to die, this is no life, constantly in pain or pooing and pouring with blood, too scared to leave the house, I had lost all my social life and confidence."

The risk of colorectal cancer increases with the extent of disease, severity of inflammation, the age of onset and duration of the disease.[xix]

All the above factors need to be reflected appropriately in the modelling and any subsequent interpretation of these.

iv) Patient population

As has been identified by clinical experts, the patient populations included in the trials selected are not fully representative of the defined population being considered within the scope of this review. The severity of disease, presence of complications and age may all affect the evaluation, particularly in terms of health utility. Patients enter the model at age 40, reflecting the median age of trial populations, yet peak diagnosis occurs at 15-25. This may have a significant effect on the results.

v) The value of biological treatments to people with moderate to severe Ulcerative Colitis for whom conventional treatments have failed

We have been overwhelmed by feedback from patients on the value of biological therapies for the treatment of their moderate-severe Ulcerative Colitis, when this has not responded to or they are intolerant of conventional treatments.

This very real practical experience is endorsed by evidence-based European Crohn's and Colitis Organisation (ECCO) guidelines and an ECCO gastroenterology group expert consensus statement: *Recommendations for the treatment of ulcerative colitis with infliximab.*

> 'If active steroid-refractory Ulcerative Colitis is confirmed, alternative therapy to induce steroid-free remission is required. Anti-TNF therapy has clear evidence of benefit in this patient group.' (ECCO)[xx]

> 'Infliximab ... for treatment of adults with moderate to severe, active ulcerative colitis (UC) unresponsive to conventional therapies. It rapidly controls symptoms, induces and sustains steroid-free remission, stimulates mucosal healing and reduces serious complications. Although infliximab tends to be reserved for patients with severe disease, it may be even more beneficial for moderate disease earlier in the disease course.'[xxi]

"I no longer panic about leaving the house. I no longer spend weeks on end in hospital. I no longer feel a burden on my family and I can actually work again. I feel like I actually have a quality of life again, I lost so many years of my young adult life because of my condition."

"I have never felt better in my life."

"I am not allowed to continue with more infusions, so I stress each day waiting for the next attack/stint in hospital, whilst I continue to have poor experiences with other medications that don't work. This is terribly frustrating knowing that there is something that will make the world of difference to my life but I am unable to receive it."

"For the first time in just over 10 years, my fiancé's symptoms ceased. She could go out without fear. She could do the most basic things in life that other people take for granted. Everyone breathed a massive sigh of relief and said a prayer of thanks for this miracle."

"Within 24 hours of the infusion, I stopped bleeding and within 48 hours I was having two comfortable bowel movements per day (reduced from 12 plus day and night). It has been life-changing. I shortly after went on holiday and, since returning, started a new job where no-one would know that, a month prior, I could hardly walk, sleep or leave the house. For me, this has been a miracle treatment."

"That was then, but this is now. Life is fun & hectic. Humira has given my family back their wife & mummy. I can laugh without pooing myself, I can tickle my children and they can tickle me back, we can go for long walks with our dog, to the theatre, for days out, whatever we want to do. I have even been working extra days at work and feel that I do a good job again."

vi) Stopping rules

a) Patients who receive anti-TNF therapy who do not respond at the end of the induction period should have their anti-TNF therapy stopped. Clear stopping rules could and should be applied after induction for these primary non-responders. This is not fully considered in the model.

b) For those who lose response during the first year of therapy (secondary non-responders) drug and anti-drug antibody levels should be used to determine whether switching to an alternative anti-TNF should be considered, or if surgery is preferable. This is not considered in the model.

c) Review at one year is likely to be a clinically and cost-effective treatment strategy, with further treatment only in those who subsequently relapse and would bring the UC recommendations into line with those for Crohn's Disease.

Stopping rules are in place for infliximab and adalimumab for Crohn's Disease and there is evidence that these are equally applicable for Ulcerative Colitis. For example:

- Molander et al (IBD 2014; 0:1-8) showed that 22/34 UC patients remained in remission after cessation, and 94% of those relapsing responded to retreatment
- Steenholdt et al (Scand J GE 2012; 47:518–527) showed that of 28 UC patients stopping whilst in clinical steroid-free remission, 75% remained in remission at 1 year and 5/7 (71%) responded to retreatment.
- Farkas et al (Scand J GE 2013; 48:1394-1398) followed 51 patients who stopped infliximab after one year, and 65% remained in remission at one year after cessation, with the majority of relapses responding to retreatment.

- Villafranca et al (JCC 2014; 8:S234-235) prospectively studied UC patients given one year of infliximab. 12 with mucosal healing at one year stopped the drug, and 75% remained in remission over 2 years follow-up. The 3 relapsing responded well to retreatment.

It seems inappropriate to model continuous anti-TNF therapy in all patients maintaining a response over the long-term when this does not reflect UK clinical practice. This assumption will substantially overestimate the true cost of treatment, in particular when placed within modelling over a lifetime horizon. We believe there is sufficient evidence to consider the impact of stopping rules on the cost-effectiveness estimates.

"I have severe pancolitis and have had the three induction doses plus another 4 doses of infliximab since the beginning of December 2013. Before that, I had been admitted to hospital almost every two months – 5 times in 2013 alone. This pattern has existed since my UC flared in 2010. It has given me my life back. I can also work and have a social life. I have gained some confidence in myself and am no longer constantly worried about urgently needing the toilet. I have not had any bleeding or diarrhoea since February and I finally feel like my gut is having a chance to heal. I am only opening my bowels between 2 and 4 times a day. I have energy, my joints and bones are generally better and my hair (which had thinned and fallen out with steroids and other meds) is growing back to its former glory."

2. Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence

As full account has not been taken of the evidence outlined above, the summaries of clinical and cost effectiveness are not considered to be reasonable at this stage. We would strongly urge that the additional evidence highlighted in this submission is given consideration and that the decision is reviewed in light of this.

3. Are the provisional recommendations a sound and suitable basis for guidance to the NHS?

The provisional recommendations are not a sound and suitable basis for guidance to the NHS. They are not in line with clinical practice and opinion and leave patients with Ulcerative Colitis in the UK in a substantially worse position in terms of treatment options compared with those with Crohn's Disease and those with Ulcerative Colitis in many other countries in the developed world.

"I am a 20 year old student. I have been steroid dependent and azathioprine treatment is no longer effective for me. In other developed countries, particularly in North America, biologic drugs are the natural next step for treating UC when immunosuppressants fail. The right drugs existed but were just out of my reach. I therefore jumped on the opportunity when I heard of a clinical trial for golimumab."

If the preliminary recommendations are upheld, this decision could condemn a clearly defined proportion of children and adults who are experiencing ongoing chronic active disease with its many debilitating and devastating impacts to life-altering surgery, which may have been avoided, at a time when they may be the most ill-prepared to deal with it. The implications of this will be significant, not just for individuals and families, but also for the NHS and wider society, in terms of education, employment and the welfare system.

"To take away my last hope of avoiding this dreadful prospect would be a bitter blow."

"If infliximab was taken away from me, I am sure I would not cope with an ileostomy."

[i] Reich KM, Chant H-J, Rezaie, H *et al.* The incidence rate of colectomy for medically refractory ulcerative colitis has declined in parallel with increasing anti-TNF use: a time-trend study. *Alimentary Pharmacology & Therapeutics*, 40: 629–638. Article first published online: 13 July 2014

[ii] Dayan B, Turner B. Role of surgery in severe ulcerative colitis in the era of medical rescue therapy. *World J Gastroenterol* 2012 Aug 7; 18(29):3833-8.

[iii] National clinical audit of inpatient care for adults with ulcerative colitis June 2014, Royal College of Physicians Clinical Effectiveness and Evaluation Unit, on behalf of the IBD Programme Steering Group. https://www.rcplondon.ac.uk/sites/default/files/adult_ibd_inpatient_care_audit_web.pdf

[iv] Mowat C, Cole A, Windsor A et al. Guidelines for the management of inflammatory bowel disease in adults. *Gut* 2011; 60:571-607.

[v] Tiainen J, Matikainen M. Health-Related Quality of Life after Ileal J-Pouch Anal Anastomosis for Ulcerative Colitis: Long-Term Results. *Scand J Gastro*. 1999; 34,(6):601-605

[vi] Berndtsson I, Oresland T. Quality of life before and after protocolectomy and IPAA in patients with ulcerative protocolitis – a prospective study. *Colorectal Dis.* 2003, March; 5(2):173-9.

[vii] Ananthakrishnan AN, Gainer VS, Cai T *et al.* Similar risk of depression or anxiety following surgery or hospitalization for Crohn's disease and ulcerative colitis. *Am J Gastroenterol.* 2013 Apr; 108(4):594-601.

[viii] Casellas F, López-Vivancos J, Casado A, and Malagelada JR. Factors affecting health related quality of life of patients with inflammatory bowel disease. *Quality of Life Research*, 2002; 11(8):775–781.

[ix] Haapamaki J. Health-Related Quality of Life, Symptoms and Comorbidity in Inflammatory Bowel Disease [Ph.D. dissertation], The Medical Faculty of the University of Helsinki, 2011.

[x] Cámara JA, Ziegler R, Begré S *et al.* The role of psychological stress in inflammatory bowel disease: quality assessment of methods of 18 prospective studies and suggestions for future research. *Digestion*. 2009;80(2):129–139.

[xi] Mawdsley, JE, Ramptom, DS. Psychological stress in IBD: new insights into pathogenic and therapeutic implications. *Gut.* 2005; 54(10):1481-1491.

[xii] Gay M *et al.* Crohn's, Colitis and Employment – from Career Aspirations to Reality. Crohn's and Colitis UK, 2011

[xiii] Cosnes J, Gowerrousseau C, Seksik P, and Cortot A. Epidemiology and natural history of inflammatory bowel diseases. *Gastroenterology*. 2011; 140(6):1785–1794.

[xiv] Graff LA[1], Walker JR, Bernstein CN. Depression and anxiety in inflammatory bowel disease: a review of comorbidity and management. Inflamm Bowel Dis. 2009 Jul; 15(7):1105-18.

[xv] Graff LA et al. Stress coping, distress and health perceptions in inflammatory bowel disease and community controls. Am J Gasterenterol. 2009. Dec; 104(12):2959-69.

[xvi] Minderhoud IM, Oldenburg B, van Dam PS et al. High prevalence of fatigue in inflammatory bowel disease is not related to adrenal corticol insufficiency. Am J Gastroenterol 2003; 98;1088-93.

[xvii] Mowat C, Cole A, Windsor A et al. Guidelines for the management of inflammatory bowel disease in adults. *Gut* 2011; 60:571-607.

[xviii] Ibid.

[xix] Cairns S et al. Guidelines for colorectal cancer screening and surveillance in moderate and high risk groups (update from 2002). Gut. 2010; 59, 666-690.

[xx] Dignass A, Lindsay J, Sturm A *et al.* Second European evidence-based consensus on the diagnosis and management of ulcerative colitis Part 2: Current management. *Journal of Crohn's and Colitis* 2012; 6:991-1030.

[xxi] Reinisch W, Van Assche G, Befrits R *et al.* Recommendations for the treatment of ulcerative colitis with infliximab: A gastroenterology expert group consensus.*Journal of Crohn's and Colitis* 2012 March; 6(2):248-258.

[xxii] Iqbal F, Zaman S, Bowley D and Vaizey C. Quality of life after restorative protocolectomy in Muslim patients. *Gut* 2014; 63:1197-1198.

4. **Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?**

As outlined above, pouch surgery can affect fertility and, as such, discriminates again young people who may not yet have a family and who are in the peak diagnosis group for this condition. Active disease that is not responding to conventional treatment is likely to force a need for surgery, so this cannot be dismissed. For certain religious groups, such as Muslims, the impact of active disease and the effects of pouch surgery may interfere with religious practices and cause particular distress, which would be alleviated by the option of biological therapy.[xxii]

Patient and public engagement

We welcome the various opportunities that exist for stakeholders to engage with this appraisal process, through consultation responses as an identified stakeholder, nomination of patient experts, ability to observe appraisal committee meetings and public consultation. However, we would like to register our concern that it remains extremely difficult to engage optimally with a process which involves commenting on a 437 page assessment report containing detailed economic modelling. There is a need for this to be communicated more clearly and accessibly to stakeholders than is currently the case and we would suggest that this could most usefully be achieved through a workshop event, where questions could be asked by stakeholders to obtain further clarification and thereby ensure all relevant factors have been identified.

Summary

- There is a clear and defined need for biological drugs to be available to people with moderate to severe Ulcerative Colitis, for whom conventional treatments have failed, using stopping rules which would bring this in line with the guidance for Crohn's Disease (TA187)
- Neither surgery or conventional treatment are appropriate comparators for biological drugs as conventional treatment has, by definition, failed and, unless by patient choice, surgery should be considered a last resort when all appropriate medical options have been explored
- Considerable uncertainties arise from the modelling in terms of:
  - lack of representativeness of the patient population being considered
  - extrapolation of short-term data to a lifetime horizon
  - lack of stopping rules
  - full costs, complications and risks of surgery
  - small sample on which health utility values are based
  - selection of conventional therapy as a comparator, when this has already failed this group of patients
- There are significant equality/diversity issues in terms of effectively compelling patients in this group to elective or potential emergency surgery, in particular for young people who have not begun a family and whose fertility may be affected, and for religious groups such as Muslims, for whom this may impact on religious practices and cause particular distress.

For further information: