NICE Multiple Technology Appraisal

Infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy (including a review of TA140 and TA262)

Submission from [redacted] British Society of Gastroenterology

Impact of surgery in ulcerative colitis (UC)

Ulcerative colitis remains a challenging condition to treat. The peak age of onset is between 15 and 30, and a subgroup of patients develop chronic treatment-refractory symptoms resulting in poor quality of life, disruption to family life, loss of employment or disrupted education, and often necessitating subtotal colectomy and ileostomy formation. Very often this surgery is needed in young people who have not yet formed relationships with future partners, where a stoma is a significant social handicap. Many will not have started a family, and the option of ileoanal pouch anastomosis is often delayed or dismissed because of the risk to fecundity as a result of pelvic surgery. For these patients there is an understandable desire to want disease control with medical therapy, therefore removing the need for surgery during critical times (school and higher education, before formation of permanent relationships, before completion of family, and at times when jobs and livelihood are threatened by chronic ill-health and sick-leave). The use of anti-TNF therapy to control UC in this situation is a precious resource, and it is hard to extrapolate from artificially uniform clinical trials with rigid inclusion criteria to measure the impact of these drugs on patients' quality of life, in comparison to the surgical alternative.

Comparison with Crohn's disease

The impact of NICE guidance on use of anti-TNF therapy differs dramatically between patients with Crohn's disease, and those with ulcerative colitis. Considering the growing evidence of common genetic factors shared by both diseases, and the clear overlap, often making clinical discrimination between the two extremely difficult, this is difficult for clinicians and patients to understand. Both diseases have subgroups of patients with chronic active symptoms refractory to conventional therapy with corticosteroids, thiopurines, methotrexate (Crohn's) or mesalazine (UC). For Crohn's however anti-TNF therapy is available, and provides control of disease in a significant proportion. For UC patients however, anti-TNF therapy is only available in those who are admitted with acute severe disease, and in whom ciclosporin is contra-indicated or ineffective.

Changes in evidence since April 2008 (NICE guidance TA140)

Since 2008, a significant amount of new data has clarified the role of infliximab in moderate to severe ulcerative colitis. Data is also available for both adalimumab and golimumab, and trial design has evolved significantly to include the recruitment of induction-therapy responders to placebo-controlled maintenance studies(1). For infliximab, long-term follow-up data from ACT 1 and 2 studies shows persistent response with low colectomy rates at up to four years(2). Colectomy rate data from ACT 1 and 2 is available(3) showing a significant reduction in week 54 colectomy rate of 10%, compared to 17% in the placebo arm. Real-life observational studies with cohorts of more than 100

patients are available from Belgium(4), France(5) and Italy(6). Controlled trial data comparing outcomes of combination therapy with azathioprine and infliximab, in comparison with either drug as monotherapy are also available in the SUCCESS study(7).

In addition, it has become clear that treatment goals beyond symptom control and improved quality of life are important: including complete mucosal healing, steroid-free status, and reduced complication rates(8). Factors indicative of improved response and remission rates to anti-TNF therapy include high C-reactive protein(8).

Availability of biosimilar drugs, with the potential to reduce significantly the costs of anti-TNF therapy are set to alter significantly the Incremental Cost Effectiveness Ratio calculations for this treatment.

Adalimumab and Golimumab

Whilst there are fewer data available in comparison to infliximab, and bearing in mind the difficulties of comparing different trials, there is high quality data with broadly similar results to infliximab in moderate to severe UC for both adalimumab(9, 10) and golimumab(1, 11).

Summary

This assessment should consider these factors as part of the proposed assessment in appendix B

1) When the comparator of surgery is used, it must be borne in mind that many young patients (particularly women) will have an ileostomy for many years, because ileoanal pouch surgery is delayed to preserve fertility

2) The benefits of anti-TNF drugs in UC will be comparable to those in Crohn's colitis and guidance should be broadly comparable

3) The impact of biosimilars in reducing drug costs must be factored in

4) The assessment must include subgroups of patients likely to respond better to therapy, thus improving the ICER

5) Combination therapy with azathioprine improves effectiveness, but was not part of the main studies for the agents under consideration. The SUCCESS data can be used to estimate the additional benefits.

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