NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

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)

Draft scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of infliximab, adalimumab and golimumab within their licensed indications for treating moderately to severely active ulcerative colitis.

Background

Ulcerative colitis is a chronic condition where inflammation develops in the large intestine. Symptoms include bloody diarrhoea, abdominal pain, weight loss, fatigue, anaemia and an urgent need to defaecate. These vary according to the extent and severity of the inflammation. Symptoms can flare up and then disappear for months or even years, but approximately 50% of people with ulcerative colitis will relapse at least once a year. Common complications of ulcerative colitis include primary sclerosing cholangitis (inflamed and damaged bile ducts), bowel cancer, osteoporosis and toxic megacolon (trapped gases in the colon, causing it to swell). Severe ulcerative colitis, in particular, is also associated with significant emotional distress.

Ulcerative colitis has a reported annual incidence in the UK of approximately 10 per 100,000 people, and a prevalence of approximately 240 per 100,000. Therefore, it is estimated that approximately 132,600 people in England and Wales are diagnosed with ulcerative colitis. About 80% of all incident cases of ulcerative colitis are mild or moderate in severity. The age of onset peaks between 15 and 30 years of age but the disease may present at all ages. Acute severe ulcerative colitis is associated with an annual mortality rate of up to 2% compared with 0.8% in the UK general population.

The British Society of Gastroenterology defines mildly active ulcerative colitis as less than 4 bowel movements daily. Moderately active ulcerative colitis is defined as more than 4 daily bowel movements but where the patient is not systemically ill. Severe ulcerative colitis is potentially life threatening and is defined as an attack in which the patient has more than 6 bowel movements daily, and is systemically ill as shown by tachycardia, fever and anaemia.

There is no cure for ulcerative colitis. The aim of treatment is to relieve symptoms during a flare-up and to maintain remission thereafter. Management of mildly to moderately active colitis involves treatment with, oral or topical aminosalicylates (sulfasalazine, mesalazine, balsalazide or

olsalazine) or corticosteroids when aminosalicylates are contraindicated or not tolerated. Oral corticosteroids or oral immunosuppressants are also added on if the disease does not respond to treatment with aminosalicylates. NICE does not recommend infliximab for treating subacute manifestations of moderately to severely active ulcerative colitis (NICE technology appraisal guidance 140). NICE was unable to appraise adalimumab for treating subacute manifestations of moderately to severely active ulcerative colitis because the manufacturer did not provide an evidence submission (NICE technology appraisal guidance 262).

NICE technology appraisal guidance 163 recommends infliximab for treating acute exacerbations of severely active ulcerative colitis when ciclosporin is contraindicated or inappropriate. A review of TA163 is not included in this appraisal, and so acute severely active ulcerative colitis is not included in this scope.

The technologies

Infliximab (Remicade, Merck Sharp & Dohme) is a chimeric monoclonal antibody that binds with high affinity to TNF-alpha, thereby neutralising its activity. It is administered by intravenous infusion. Infliximab has a UK marketing authorisation for the treatment of moderately to severely active ulcerative colitis in adult patients who have had an inadequate response to conventional therapy including corticosteroids and mercaptopurine or azathioprine, or who are intolerant to or have medical contraindications for such therapies. Infliximab also has a UK marketing authorisation for the treatment of severely active ulcerative colitis, in children and adolescents aged 6 to 17 years, who have had an inadequate response to conventional therapy including corticosteroids and mercaptopurine or azathioprine, or who are intolerant to or have medical contraindications for such therapies.

Adalimumab (Humira, AbbVie) inhibits the activity of TNF-alpha. It is a fully human recombinant monoclonal IgG1 antibody specific for TNF-alpha. It is administered by subcutaneous injection. Adalimumab has a UK marketing authorisation for the treatment of moderately to severely active ulcerative colitis in adult patients who have had an inadequate response to conventional therapy including corticosteroids and mercaptopurine or azathioprine, or who are intolerant to or have medical contraindications for such therapies.

Golimumab (Simponi, Merck Sharp & Dohme) is a fully humanised monoclonal antibody that inhibits TNF-alpha. It is administered subcutaneously. Golimumab does not currently have a UK marketing authorisation for use in ulcerative colitis. It has been studied in clinical trials, compared with placebo, in adults with moderately to severely active ulcerative colitis who have had an inadequate response to conventional therapy including corticosteroids and mercaptopurine or azathioprine, or who are intolerant to or have medical contraindications for such therapies.

Intervention(s)	For adults: • adalimumab • infliximab • golimumab For children and adolescents: • infliximab
Population(s)	People with moderately to severely active ulcerative colitis, whose disease has responded inadequately to conventional therapy including corticosteroids and mercaptopurine or azathioprine, or who are intolerant of or have medical contraindications to such therapies
Comparators	Adalimumab, infliximab and golimumab should be compared with each other and with standard clinical management which may include a combination of aminosalicylates (sulfasalazine, mesalazine, balsalazide or olsalazine), corticosteroids (beclomethasone, budesonide, hydrocortisone or prednisolone) and immunosuppressants (mercaptopurine or azathioprine) and surgical intervention
Outcomes	The outcome measures to be considered include: • mortality • measures of disease activity • rates of and duration of response, relapse and remission • rates of hospitalisation • rates of surgical intervention • time to surgical intervention • adverse effects of treatment (including leakage and infections following surgery) • health-related quality of life

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any patient access schemes for the intervention or comparator technologies should be taken into account.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 140, April 2008, 'Infliximab for subacute manifestations of ulcerative colitis'. Technology Appraisal No. 163, December 2008, 'Infliximab for the treatment of acute exacerbations of ulcerative colitis'. Terminated Technology Appraisal No. 262, July 2012, 'Adalimumab for the treatment of moderate to severe ulcerative colitis'. Related Guidelines: Clinical Guideline No. 166, June 2013, 'Ulcerative colitis: Management in adults, children and young people'.

Questions for consultation

Have the most appropriate comparators for infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis been included in the scope?

Should ciclosporin be included as a comparator?

Are there any subgroups of people in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

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 the

proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which infliximab, adalimumab are licensed and golimumab 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 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.

Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.