NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Tofacitinib for moderately to severely active ulcerative colitis

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of tofacitinib within its marketing authorisation for treating moderately to severely active ulcerative colitis.

Background

Ulcerative colitis is the most common inflammatory bowel disease. The cause of ulcerative colitis is unknown. Hereditary, infectious and immunological factors have been proposed as possible causes. It can develop at any age, but peak incidence is between the ages of 15 and 25 years, with a second, smaller peak between 55 and 65 years. It has been estimated that around 146,000 people in England have ulcerative colitis, of whom about 52% have moderate to severe disease.

Ulcerative colitis usually affects the rectum, and a variable extent of the colon proximal to the rectum. The symptoms of ulcerative colitis are bloody diarrhoea, colicky abdominal pain, urgency and tenesmus. Some patients may have extra-intestinal manifestations involving joints, eyes, skin and liver. Ulcerative colitis is a lifelong disease that is associated with significant morbidity; symptoms can relapse and then go into remission for months or even years. Around 50% of people with ulcerative colitis will have at least one relapse per year. About 80% of these are mild to moderate and about 20% are severe. Complications of ulcerative colitis may include haemorrhage, perforation, stricture formation, abscess formation and anorectal disease. People with long-standing disease have an increased risk of bowel cancer.

The severity of ulcerative colitis may be classified based on criteria such as the Mayo Scoring System. It has 4 components: stool frequency, rectal bleeding, findings at endoscopy (typically sigmoidoscopy), and a physician's global assessment. It ranges from 0 to 12, with higher scores indicating more severe disease. A Mayo score of 6 to 12 defines moderate to severely active ulcerative colitis. It can be used for both initial evaluation and monitoring treatment response. Remission of the disease is defined by a total Mayo score of 2 points or lower, with no individual sub-score exceeding one.[1] NICE clinical guideline 166 on ulcerative colitis equates 'subacute ulcerative colitis' to moderately to severely active ulcerative colitis, which would normally be managed in an outpatient setting and does not require hospitalisation or the consideration of urgent surgical intervention. The scope of this appraisal does not include severe ulcerative colitis that is a medical emergency requiring intensive inpatient treatment.

The aim of treatment in active disease is to address symptoms of urgency, frequency and rectal bleeding, and thereafter to maintain remission. NICE recommendations for managing moderately to severely active ulcerative colitis are found in NICE clinical guideline 166. Initial management depends on clinical severity, extent of disease and the person's preference, and may include corticosteroids, or topical or oral aminosalicylates (sulfasalazine, mesalazine, balsalazide or olsalazine). If the disease does not adequately respond to oral corticosteroids (beclometasone, budesonide, hydrocortisone or prednisolone) then an immunosuppressant (such as mercaptopurine or azathioprine) may be considered. NICE technology appraisal 329 recommends infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis in adults whose disease has responded inadequately to conventional therapy including corticosteroids and mercaptopurine or azathioprine, or who cannot tolerate, or have medical contraindications for, such therapies. NICE technology appraisal 342 recommends vedolizumab for treating moderately to severely active ulcerative colitis. Colectomy (with the creation of either an ileostomy or an ileo-anal pouch) is a treatment option for some patients, to improve the quality of life in chronic or treatment-refractory active disease or to treat cancer or pre-cancerous changes.

The technology

Tofacitinib (Xeljanz, Pfizer) is a Janus kinase (JAK) inhibitor, and is a targeted synthetic small molecule. Janus kinases are intracellular enzymes that transmit signals arising from cytokine or growth factor-receptor interactions on the cellular membrane to influence cellular processes of creating new blood cells in the body (hematopoiesis) and immune cell function. It is administered orally.

Tofacitinib does not currently have a marketing authorisation in the UK for treating moderately to severely active ulcerative. It has been studied in clinical trials as monotherapy in adults with moderate to severe ulcerative colitis (defined based on the Mayo Scoring System) whose disease failed to respond or who could not tolerate oral corticosteroids, azathioprine/mercaptopurine, or a TNF-alpha inhibitor.

Intervention	Tofacitinib
Population	People with moderately to severely active ulcerative colitis who are intolerant of, or whose disease has had an inadequate response or loss of response to conventional therapy (oral corticosteroids and/or immunosuppressants) or a TNF-alpha inhibitor
Comparators	• TNF-alpha inhibitors (infliximab, adalimumab and golimumab) • Vedolizumab • Conventional therapies, without biological treatments

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 • achieving mucosal healing • adverse effects of treatment • 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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out. 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 will be taken into account. For the comparators, the availability and cost of biosimilars should be taken into account.

Other considerations	If evidence allows the following subgroups will be considered: • people who have been previously treated with one or more biologics and people who have not received prior biologics therapy. Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: 'Vedolizumab for treating moderately to severely active ulcerative colitis' (2015).Technology appraisal guidance TA342. Review date June 2018. 'Infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy' (2015). Technology appraisal guidance TA329. Review date February 2018. Related Guidelines: Ulcerative colitis: management .Clinical guideline CG166 Published date: June 2013. Surveillance review decision – June 2017 – planning an update Related Interventional Procedures: 'Leukapheresis for inflammatory bowel disease' (2005). NICE interventional procedures guidance 126. 'Transanal total mesorectal excision of the rectum' (2015) NICE interventional procedures guidance 514. Related NICE Pathways: Ulcerative colitis (2017) NICE pathway http://pathways.nice.org.uk/
Related National Policy	NHS England (2013) 2013/14 NHS Standard contract for colorectal: complex (adult) particulars, schedule 2- the services, A- Service specifications. Reference: A08/S/c The Health Foundation (2009) Implementing shared the UK A report for the Health Foundation **National Service Frameworks** Long Term Conditions (including neurological) - archived **Other policies**

	Department of Health (2016) NHS outcomes framework 2016 to 2017 Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1, 2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

References

1 Rutgeerts P, Sandborn W J, Feagan B G et al. (2005) Infliximab for Induction and Maintenance Therapy for Ulcerative Colitis. N Engl J Med 353:2462–2476.