Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Etrasimod for treating moderately to severely active ulcerative colitis

Final scope

Final remit/evaluation objective

To appraise the clinical and cost effectiveness of etrasimod 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 ulcerative colitis affects at least 1 in 227 people, of whom about 52% of people have moderate to severe disease.[1,2]

Ulcerative colitis can cause inflammation in the inner lining of the large intestine. This is usually restricted to the mucosal surface. This usually affects the rectum, and extends proximally throughout the colon. The symptoms of ulcerative colitis include bloody diarrhoea, colicky abdominal pain, urgency, ulceration, tenesmus, fatigue, and anaemia. Up to 50% of people with ulcerative colitis will experience extra-intestinal manifestations involving joints, eyes, skin, and liver.[2] Ulcerative colitis is associated with significant morbidity; symptoms can have a debilitating impact on quality of life and daily life, including physical, social, and mental wellbeing. It is a lifelong disease, and symptoms can recur, or the disease can go into remission for months or even years.

Ulcerative colitis can be defined as mild or moderate to severe. Around 50% of people with ulcerative colitis will have at least one relapse per year.[3] About 80% of these are mild to moderate and about 20% are severe.[3] 15-25% of people with ulcerative colitis will require hospitalisation due to acute severe colitis.[4] Complications of ulcerative colitis may include haemorrhage, bowel perforation, stricture formation, abscess formation and anorectal disease. Some people may also develop primary sclerosing cholangitis, osteoporosis, and toxic megacolon. People with long-standing disease have an increased risk of bowel cancer.

The aim of treatment in active disease is to improve quality of life through addressing symptoms of bloody diarrhoea, urgent need to defecate and abdominal pain, and thereafter to maintain remission. Initial management depends on clinical severity, extent of disease and the person's preference, and may include aminosalicylates (sulfasalazine, mesalazine, balsalazide or olsalazine), corticosteroids (beclometasone, budesonide, hydrocortisone, or prednisolone) and biologics. An immunosuppressant (such as mercaptopurine or azathioprine) may be considered to maintain remission if aminosalicylates fail to do so.

Treatments appraised by NICE for moderately to severely active ulcerative colitis include:

- 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 severe active ulcerative colitis in adults.

- NICE technology appraisal 547 recommends tofacitinib for treating moderately to severely active ulcerative colitis in adults when conventional therapy or a biological agent cannot be tolerated, or the disease has responded inadequately or lost response to treatment.

- NICE technology appraisal 633 recommends ustekinumab for treating moderately to severely active ulcerative colitis in adults when conventional therapy or a biological agent cannot be tolerated, or the disease has responded inadequately or lost response to treatment, only if a tumour necrosis factor-alpha inhibitor has failed, cannot be tolerated or is not suitable.

- NICE technology appraisal 792 recommends filgotinib for treating moderately to severely active ulcerative colitis in adults when conventional or biological treatment cannot be tolerated, or the disease has not responded well enough or has stopped responding to these treatments

- NICE technology appraisal 828 recommends ozanimod for treating moderately to severely active ulcerative colitis in adults when conventional treatment cannot be tolerated or is not working well enough and infliximab is not suitable, or biological treatment cannot be tolerated or is not working well enough.

- NICE technology appraisal 856 recommends upadacitinib for treating treating moderately to severely active ulcerative colitis in adults when conventional or biological treatment cannot be tolerated, or if the condition has not responded well enough or has stopped responding to these treatments.

The technology

Etrasimod (brand name unknown, Pfizer) does not currently have a marketing authorisation in the UK for moderately to severely active ulcerative colitis. It has been studied in clinical trials compared with placebo in people with moderately to severely active ulcerative colitis who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent.

Intervention(s)	Etrasimod
Population(s)	People with moderately to severely active ulcerative colitis when conventional therapy or a biological agent cannot be tolerated, or the disease has responded inadequately or lost response to treatment

Comparators	At least 1 of the following treatments, according to NICE guidance: • Ozanimod • JAK inhibitors (tofacitinib, filgotinib and upadacitinib) • TNF-alpha inhibitors (infliximab, adalimumab and golimumab) • Ustekinumab • Vedolizumab • Mirikizumab (subject to NICE evaluation)
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 • endoscopic healing • endoscopic remission combined with histological improvement • corticosteroid-free remission • achieving mucosal healing • adverse effects of treatment • health-related quality of life.
Economic analysis	This technology has been selected to be appraised as a cost-comparison. The time horizon should be sufficient to reflect any differences in costs between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention and comparator technologies will be taken into account.

Other considerations	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	**Related Technology Appraisals:** Upadacitinib for treating moderately to severely active ulcerative colitis (2023) NICE technology appraisal guidance TA856. Ozanimod for treating moderately to severely active ulcerative colitis (2022). NICE technology appraisals guidance TA828. Filgotinib for treating moderately to severely active ulcerative colitis (2022) NICE technology appraisals guidance TA792. Ustekinumab for treating moderately to severely active ulcerative colitis (2020). NICE technology appraisals guidance TA633. Tofactinib for treating moderately to severely active ulcerative colitis (2018). NICE technology appraisals guidance TA547. Vedolizumab for treating moderately to severely active ulcerative colitis (2015). NICE technology appraisals guidance TA342. Infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy (2015) NICE technology appraisal guidance 329. **Related technology appraisals in development:** Mirikizumab for previously treated moderately to severely active ulcerative colitis. NICE technology appraisal [ID3973]. Publication date to be confirmed. Risankizumab for previously treated moderately to severely active ulcerative colitis in people aged 16 and over. NICE technology appraisal [ID6209]. Publication date to be confirmed. **Related Guidelines:** Ulcerative colitis: management (2019) NICE guideline NG130. **Related Interventional Procedures:** Leukapheresis for inflammatory bowel disease (2005). NICE interventional procedures guidance 126. **Related Quality Standards:** Inflammatory bowel disease (2015). NICE quality standard 81

Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2017, updated 2023) Prescribed specialised services manual Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1, 2

References

1. Crohn's and Colitis UK (2017) Ulcerative Colitis. Accessed November 2022.
2. IBD UK (2021) Crohn's and Colitis Care in the UK: The Hidden Cost and a Vision for Change. Accessed November 2022.
3. National Institute for Health and Care Excellence (2014) Quality standards and indicators Briefing Paper. Accessed November 2022.
4. IBD UK (2022) Management of acute severe colitis. Accessed November 2022.