Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Etrasimod for treating moderately to severely active ulcerative colitis

Draft scope

Draft 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 between 1 in 200 and 1 in 420 people in England have ulcerative colitis, of whom about 52% 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, pain, urgency, ulceration, tenesmus, fatigue, and anaemia. Up to 50% will experience extra-intestinal manifestations involving joints, eyes, skin, and liver.[3] 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.[4] About 80% of these are mild to moderate and about 20% are severe.[4] 15-25% of people with ulcerative colitis will require hospitalisation due to acute severe colitis.[5] 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 address 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.

Current treatment for moderately to severely active ulcerative colitis also includes:

- 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

For people admitted to hospital with acute severe ulcerative colitis, NICE guideline [NG130] recommends offering intravenous corticosteroids to induce remission and assessing the need for surgery. Surgery may be considered as emergency treatment for severe ulcerative colitis that does not respond to drug treatment. People may also choose to have elective surgery for unresponsive or frequently relapsing disease that is affecting their quality of life. The scope of this appraisal does not include severe ulcerative colitis that is a medical emergency requiring intensive inpatient treatment.

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 as an induction therapy 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 who have had an inadequate response, loss of response or were intolerant to a previous biologic agent or conventional therapy

Subgroups	If the evidence allows the following subgroups will be considered: • people who have been previously treated with 1 or more biologics; • and people who have not received a prior biologic.
Comparators	• TNF-alpha inhibitors (infliximab, adalimumab and golimumab) • Tofacitinib • Ustekinumab • Vedolizumab • Filgotinib • Ozanimod (subject to ongoing NICE appraisal) • Upadacitinib (subject to ongoing NICE appraisal) • Conventional therapies (including aminosalicylates, oral corticosteroids and/or immunomodulators), 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 • 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	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 commercial arrangements for the intervention, comparator and subsequent treatment 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:** Filgotinib for treating moderately to severely active ulcerative colitis (2022) Technology appraisal TA792. Review date: 2025. Ustekinumab for treating moderately to severely active ulcerative colitis (2020). Technology appraisal TA633. Review date: 2023. Tofactinib for treating moderately to severely active ulcerative colitis (2018). Technology appraisal TA547. Review date: November 2021. Vedolizumab for treating moderately to severely active ulcerative colitis (2015). Technology appraisal TA342. Review date: June 2018. Infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy (2015) NICE technology appraisal guidance 329Review decision: static list (July 2018) **Appraisals in development (including suspended appraisals):** Ozanimod for treating moderately to severely active ulcerative colitis NICE technology appraisals guidance [ID3841]. Publication date: September 2022

	Upadacitinib for treating moderately to severely active ulcerative colitis NICE technology appraisal guidance [ID3953] Publication expected January 2023 Etrolizumab for treating moderately to severely active ulcerative colitis NICE technical appraisals guidance [ID3827]. Publication date: TBC Mirikizumab for previously treated moderately to severely active ulcerative colitis. Proposed NICE technology appraisal [ID3973]. Publication date to be confirmed. **Related Guidelines:** Ulcerative colitis: management. NICE guideline NG130. Published date: May 2019. Review date: TBC. **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 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 (2018/2019) NHS manual for prescribed specialist services (2018/2019) Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1, 2

Questions for consultation

Have all relevant comparators for etrasimod been included in the scope? Which treatments are considered to be established clinical practice in the NHS for ulcerative colitis? Are treatments given in combination in clinical practice, and if so, which combination treatments are used?

Are the outcomes listed appropriate?

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

Do you consider etrasimod 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 etrasimod 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.
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 etrasimod 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

NICE's health technology evaluations: the manual states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost-comparison methodology for this topic?

- Is etrasimod likely to be similar in its clinical efficacy and resource use to any of the comparators? Or in what way is it different to the comparators?

- Will etrasimod be used in the same place in the treatment pathway as the comparators?

- Overall, is etrasimod likely to offer similar or improved health benefits compared with the comparators?

- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. Hamilton B, Green H, Heerasing N, et al. Incidence and prevalence of inflammatory bowel disease in Devon, UK Frontline Gastroenterology 2021;12:461-470. Accessed August 2022.

2. Crohn's and Colitis UK (2017) Ulcerative Colitis. Accessed August 2022.

3. IBD UK (2021) Crohn's and Colitis Care in the UK: The Hidden Cost and a Vision for Change. Accessed August 2022.

4. National Institute for Health and Care Excellence (2014) Quality standards and indicators Briefing Paper. Accessed August 2022.

5. IBD UK (2022) Management of acute severe colitis. Accessed August 2022.