NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Mirikizumab for treating moderately to severely active ulcerative colitis

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of mirikizumab within its marketing authorisation for treating moderately to severely active ulcerative colitis after failed prior therapy.

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 severely 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.

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

Mirikizumab is a humanized monoclonal antibody that inhibits the activity of IL-23, a cytokine that plays a key role in the stimulation of many innate immune cells that are important in the pathogenesis of chronic inflammatory diseases. It is administered intravenously.

Mirikizumab does not currently have a marketing authorisation in the UK for moderately to severely active ulcerative colitis. It has been studied in a clinical trial compared with placebo as an induction therapy in 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 biologic agent (such as a TNF-alpha inhibitor or vedolizumab), and as continued maintenance therapy in people whose disease responded to initial treatment.

Intervention(s)	Mirikizumab

Population(s)	Adults with moderately to severely active ulcerative colitis who are intolerant of, or whose disease has had an inadequate response, or loss of response to previous biologic therapy (such as a TNF-alpha inhibitor or vedolizumab), or conventional therapy (oral corticosteroids and/or immunomodulators).
Subgroups	• People who have been previously treated with 1 or more biologics. • People who have not received a prior biologic.
Comparators	• TNF-alpha inhibitors (infliximab, adalimumab and golimumab) • Tofacitinib • Ustekinumab • Vedolizumab • Filgotinib (subject to ongoing NICE appraisal) • Ozanimod (subject to ongoing NICE appraisal) • Upadacitinib (subject to ongoing NICE appraisal) • 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 (including readmission) • rates of surgical intervention • endoscopic healing • mucosal healing (combines endoscopic improvement and histological remission) • corticosteroid-free remission • 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	The availability and cost of biosimilar products should be taken into account. 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:** 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: 2021. Vedolizumab for treating moderately to severely active ulcerative colitis (2015). Technology appraisal TA342. Review date: 2018. Infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy (2015). Technology appraisal TA329. Review date: TBC. **Appraisals in development (including suspended appraisals):** Filgotinib for treating moderately to severely active ulcerative colitis NICE technology appraisals guidance [ID3736]. Publication date: June 2022

	Etrolizumab for treating moderately to severely active ulcerative colitis NICE technical appraisals guidance [ID3827]. Publication date: TBC Ozanimod for treating moderately to severely active ulcerative colitis. NICE technical appraisals guidance [ID3841]. Publication date: September 2022 Upadacitinib for treating moderately to severely active ulcerative colitis. NICE technical appraisals guidance [ID3841]. Publication date: January 2023 **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 NICE Pathways: Ulcerative colitis overview (2019). NICE pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2013) 2013/14 NHS standard contract for colorectal: complex (adult) particulars, schedule 2- the services, A - service specifications. Reference: A08/S/c Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 and 2 https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Where do you consider mirikizumab will fit into the existing care pathway for ulcerative colitis?

Are all relevant comparators included in the scope?

Would mirikizumab be a candidate for managed access?

Do you consider mirikizumab 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 mirikizumab can result in any potential 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 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 mirikizumb 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 the new technology likely to be similar in its clinical efficacy and resource use to any of 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. Crohn's and Colitis UK – About Crohn's and Colitis, Ulcerative Colitis [accessed May 2022]

2. Office for National Statistics – population estimates [accessed May 2022]

3. National Institute for Health and Care Excellence. Tofacitinib for moderately to severely active ulcerative colitis [Accessed May 2022]

4. National Institute for Health and Care Excellence, Quality standards and indicators; Briefing Paper 2014 [accessed May 2022].