NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Upadacitinib for treating moderately to severely active ulcerative colitis

Final scope

Final remit/appraisal objective

To appraise the clinical and cost effectiveness of upadacitinib 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.

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

Upadacitinib (Rinvoq, AbbVie) is a selective and reversible, second-generation Janus kinase (JAK) inhibitor that blocks the JAK-signal transducer and activator of transcription (STAT) pathway and inflammatory responses. It is administered orally.

Upadacitinib 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 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 (a TNF-alpha inhibitor, ustekinumab or vedolizumab), and as continued maintenance therapy in people whose disease responded to initial treatment.

Intervention(s)	Upadacitinib
Population(s)	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

Comparators	• TNF-alpha inhibitors (adalimumab, golimumab and infliximab) • Tofacitinib • Ustekinumab • Vedolizumab • Filgotinib (subject to ongoing NICE appraisal) • Ozanimod (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 (including readmission) • 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. The availability of any managed access arrangement for the intervention will be taken into account.

Other considerations	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. 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 and NICE Pathways	**Related Technology Appraisals** Ustekinumab for treating moderately to severely active ulcerative colitis (2020) Technology appraisal guidance TA633. Review date: 2023. Tofacitinib for treating moderately to severely active ulcerative colitis (2018) Technology appraisal guidance TA547. Review date: to be confirmed. Vedolizumab for treating moderately to severely active ulcerative colitis (2015) Technology appraisal guidance TA342. Review date: to be confirmed. 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: to be confirmed. **Appraisals in development** Filgotinib for treating moderately to severely active ulcerative colitis. NICE technology appraisals guidance [ID3736]. Publication expected June 2022. Ozanimod for treating moderately to severely active ulcerative colitis NICE technology appraisals guidance [ID3841]. Publication expected September 2022. Etrolizumab for treating moderately to severely active ulcerative colitis. Proposed NICE technology appraisal [ID3827]. Publication date to be confirmed. 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: to be confirmed.

	Related Interventional Procedures Leukapheresis for inflammatory bowel disease (2005) NICE interventional procedures guidance 126. Transanal total mesorectal excision for rectal cancer (2021) NICE interventional procedures guidance 713. **Related Quality Standards** Inflammatory bowel disease (2015) NICE quality standard 81.
Related National Policy	NHS England (2019) The 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, 2 NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019)

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