NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Upadacitinib for previously treated moderately to severely active Crohn's disease

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of upadacitinib within its marketing authorisation for treating previously treated moderately to severely active Crohn's disease.

Background

Crohn's disease is a chronic inflammatory condition of the gastrointestinal tract (gut) that may affect any part of the gut from the mouth to the anus. People with Crohn's disease have recurrent relapses, with acute exacerbations ('flares') in between periods of remission or less active disease. These flares may affect any part of the gut and are defined by location (terminal ileal, colonic, ileocolic, upper gastrointestinal), or by the pattern of the disease (inflammatory, fistulising, or stricturing).

The clinical features of Crohn's disease are variable and are determined partly by the site of the disease. Common symptoms include diarrhoea, abdominal pain, extreme tiredness, unintended weight loss and blood and mucus in stools. Other symptoms may include fever, nausea, vomiting, arthritis, inflammation and irritation of the eyes, mouth ulcers and areas of painful, red and swollen skin.

Crohn's disease can be complicated by the development of strictures (a narrowing of the intestine), obstructions, fistulae and perianal disease. Other complications include acute dilation, perforation and massive haemorrhage, and carcinoma of the small bowel or colon.

Crohn's disease currently affects 1 in 650 people in the UK and estimates suggest that there are at least 115,000 people in the UK with Crohn's disease[1]. It most often appears between the ages of 10 and 40, however, it may affect people of any age[2]. The condition has a debilitating impact on the daily lives and quality of life of those affected, including mental health and wellbeing, education, employment and relationships.

Crohn's disease is not medically or surgically curable. Treatment aims to reduce symptoms, promote mucosal healing and maintain or improve quality of life while minimising drug-related toxicity. Clinical management depends on disease activity, site, behaviour of disease, response to previous treatments, side-effect profiles of treatments and extra-intestinal manifestations, such as uveitis and arthritis.

NICE clinical guideline 129 recommends monotherapy with a glucocorticosteroid (prednisolone, methylprednisolone or intravenous hydrocortisone) to induce remission in people with a first presentation or a single inflammatory exacerbation of Crohn's disease in a 12-month period. Budesonide or 5-aminosalicylates are

considered for some people who decline, cannot tolerate or in whom a conventional corticosteroid is contraindicated. When 2 or more inflammatory exacerbations are experienced in a 12-month period, azathioprine, mercaptopurine and methotrexate may be considered as add-on treatments to conventional glucocorticosteroids or budesonide to induce remission of Crohn's disease.

NICE technology appraisal 187 recommends infliximab and adalimumab as treatment options for adults with severe active Crohn's disease whose disease has not responded to conventional therapy (including immunosuppressive and/or corticosteroid treatments), or who are intolerant of or have contraindications to conventional therapy.

NICE technology appraisal 352 recommends vedolizumab as an option for treating moderately to severely active Crohn's disease if a tumour necrosis factor‑alpha inhibitor has failed, cannot be tolerated or is contraindicated.

NICE technology appraisal 456 recommends ustekinumab as an option for treating moderately to severely active Crohn's disease for adults who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a tumour necrosis factor-alpha inhibitor, or have medical contraindications to such therapies.

NICE clinical guideline 129 states that in addition to pharmacological treatment, between 50 and 80% of people with Crohn's disease will require surgery during the course of their disease. The main reasons for surgery are strictures causing obstructive symptoms, lack of response to medical therapy, and complications such as fistulae and perianal disease.

The technology

Upadacitinib (Rinvoq, AbbVie) is a selective and reversible Janus-kinase (JAK) 1 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 treating Crohn's disease. It has been studied in clinical trials compared with placebo in adults with moderate to severe Crohn's disease who have inadequately responded to or are intolerant to conventional therapy and/or biologic therapy. Upadacitinib does have a marketing authorisation in the UK for moderate to severe active rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and moderate to severe atopic dermatitis.

Intervention	Upadacitinib
Population	People with previously treated moderately to severely active Crohn's disease
Subgroups	If evidence allows, subgroups considering the location of Crohn's disease (Ileal, colonic and perianal) will be considered

Comparators	• Tumour necrosis factor-alpha inhibitors (infliximab and adalimumab) • Vedolizumab • Ustekinumab For people for whom tumour necrosis factor-alpha inhibitors, vedolizumab and ustekinumab have been ineffective, are contraindicated or are not tolerated: • Best supportive care
Outcomes	The outcome measures to be considered include: • disease activity (remission, response, relapse) • mucosal healing • surgery • hospitalisation rates • 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. 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 and cost of biosimilar and generic products should 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:** 'Darvadstrocel for treating complex perianal fistulas in Crohn's disease' (2019). NICE technology appraisal 556. Review date 2022. 'Ustekinumab for moderately to severely active Crohn's disease after previous treatment' (2017). NICE technology appraisal 456. Review date 2020. 'Vedolizumab for treating moderately to severely active Crohn's disease after prior therapy' (2015). NICE technology appraisal 352. Review date August 2018. 'Infliximab and adalimumab for the treatment of Crohn's disease' (2010). NICE technology appraisal 187. Guidance on static list. **Related appraisals in development:** 'Risankizumab for previously treated moderately to severely active Crohn's disease' NICE technology appraisal guidance [ID3986]. Publication date to be confirmed. **Related Guidelines:** 'Crohn's disease: management' (2019). NICE clinical guideline 129. Review date 2017. 'Irritable bowel syndrome in adults: diagnosis and management' (2017). NICE guideline 61. **Related Interventional Procedures:** 'Bioprosthetic plug insertion for anal fistula' (2019). NICE interventional procedure 662. 'Endoscopic ablation for an anal fistula' (2019). NICE interventional procedure 645. **Related Quality Standards:** 'Irritable bowel syndrome in adults' (2016). NICE quality standard 114. '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). Chapter 101, severe intestinal failure service (adults) NHS England 2017. NHS Medicines for Children's Policy

References

1) Crohn's disease: management (2019) NICE guideline 129

2) NHS Choices. (2021) Crohn's disease: Overview. Accessed August 2022.

