

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

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

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of risankizumab within its marketing authorisation for 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, fatigue, anaemia, 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 UK¹. It most often appears between the ages of 10 and 40, however, it may affect people of any age². 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, frequency, delivery and side-effect profiles of treatments, long term safety, as well as impact on other co-morbidities and extra-intestinal manifestations, such as uveitis, skin manifestations and arthritis.

[NICE 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

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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 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

Risankizumab (Skyrizi, AbbVie) is a humanised IgG1 monoclonal antibody that selectively binds with high affinity to the p19 subunit of interleukin-23, which prevents activation of the immune system which subsequently reduces inflammation. It is administered in induction by intravenous infusion followed by subcutaneous maintenance injection.

Risankizumab does not currently have a marketing authorisation in the UK for treating Crohn's disease. It is currently being studied in clinical trials in comparison with placebo in people 16 years and over diagnosed with moderate to severe Crohn's disease and whose condition does not tolerate or respond to biological therapy. These trials assess its use as a subcutaneous maintenance injection with an intravenous induction. Risankizumab does have a marketing authorisation in the UK for moderate to severe plaque psoriasis and active psoriatic arthritis.

Intervention(s)	Risankizumab
Population(s)	People with previously treated moderately to severely active Crohn's disease

Comparators	<ul style="list-style-type: none"> • Tumour necrosis factor-alpha inhibitors (infliximab and adalimumab; used in line with NICE guidance) • Vedolizumab (used in line with NICE guidance) • Ustekinumab (used in line with NICE guidance) <p>For people for whom tumour necrosis factor-alpha inhibitors, vedolizumab and ustekinumab have been ineffective, are contraindicated or are not tolerated:</p> <ul style="list-style-type: none"> • Best supportive care
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • disease activity (remission, response, relapse) • mucosal healing • surgery • adverse effects of treatment • health-related quality of life.
Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements in place for the intervention, comparator or subsequent treatment technologies will be taken into account.</p>
Other considerations	<p>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.</p> <p>If evidence allows, the following subgroups may be considered:</p> <ul style="list-style-type: none"> • Location of Crohn's disease (ileal, colonic and perianal) <p>The availability and cost of biosimilars should be taken into consideration.</p>
Related NICE recommendations	<p>Related Technology Appraisals:</p> <p>'Darvadstrocel for treating complex perianal fistulas in Crohn's disease' (2019). NICE technology appraisal 556.</p>

	<p>Review date 2022.</p> <p>'Ustekinumab for moderately to severely active Crohn's disease after previous treatment' (2017). NICE technology appraisal 456. Review date to be confirmed.</p> <p>'Vedolizumab for treating moderately to severely active Crohn's disease after prior therapy' (2015). NICE technology appraisal 352. Review date to be confirmed.</p> <p>'Infliximab and adalimumab for the treatment of Crohn's disease' (2010). NICE technology appraisal 187. Guidance on static list.</p> <p>Related Guidelines:</p> <p>'Crohn's disease: management' (2019). NICE guideline 129. Review date to be confirmed.</p> <p>Related Interventional Procedures:</p> <p>'Bioprosthetic plug insertion for anal fistula' (2019). NICE interventional procedure 662.</p> <p>'Endoscopic ablation for an anal fistula' (2019). NICE interventional procedure 645.</p>
Related National Policy	<p>NHS England 2019. The NHS long term plan</p> <p>NHS England 2018. Manual for prescribed specialised services 2018/19. Chapter 101, severe intestinal failure service (adults) prescribed-specialised-services-manual.pdf (england.nhs.uk)</p> <p>NHS England 2017. NHS Medicines for Children's Policy</p>

References

- 1) Crohn's and Colitis UK (2019) [What is Crohn's disease?](#) Accessed November 2021.
- 2) NHS Choices. (2021) [Crohn's disease: Overview](#). Accessed November 2021.