NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

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

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of risankizumab 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. Less common symptoms 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[1]. It most often appears between the ages of 10 and 40, however, it may affect people of any age[2].

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

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 as a 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.

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

Comparators	• Conventional therapy (which can include drug treatment with conventional glucocorticosteroids alone or in combination with azathioprine, mercaptopurine or methotrexate; aminosalicylates; budesonide alone or in combination with azathioprine, mercaptopurine or methotrexate) • Tumour necrosis factor-alpha inhibitors (infliximab and adalimumab) • Vedolizumab • Ustekinumab
Outcomes	The outcome measures to be considered include: • disease activity (remission, response, relapse) • mucosal healing • surgery • 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 patient access schemes for the intervention or comparator 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. If evidence allows, the following subgroups may be considered: • People who have not previously received a tumour necrosis factor-alpha inhibitors; • People for whom at least 1 tumour necrosis factor-alpha inhibitor has failed; • People for whom tumour necrosis factor-alpha inhibitors are not suitable because of intolerance or contraindication. • Location of Crohn's disease (Ileal, colonic and perianal) The availability and cost of biosimilars should be taken into consideration.
Related NICE recommendations and NICE Pathways	**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 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 NICE Pathways:** Crohn's disease (2020) NICE Pathway
Related National Policy	NHS England 2019. The NHS long term plan 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) NHS England 2017. NHS Medicines for Children's Policy

Questions for consultation

At what point in the treatment pathway would risankizumab be used? Would it be used as an alternative to:

- Tumour necrosis factor-alpha inhibitors (infliximab and adalimumab); or
- Vedolizumab and ustekinumab

Or would risankizumab be used after these treatments already available in the NHS?

Have all relevant comparators for risankizumab been included in the scope? Which treatments are considered to be established clinical practice in the NHS for Crohn's disease?

Are the outcomes listed appropriate?

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

Where do you consider risankizumab will fit into the existing NICE pathway, Crohn's disease?

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 risankizumab 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.

Do you consider risankizumab 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 risankizumab 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.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which 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 (2019) What is Crohn's disease? Accessed November 2021.
2) NHS Choices. (2021) Crohn's disease: Overview. Accessed November 2021.