

Health Technology Briefing October 2022

Risankizumab for moderate to severe ulcerative colitis

Company/Developer

AbbVie

New Active Substance

Significant Licence Extension (SLE)

NIHRIO ID: 23880

NICE ID: 10636

UKPS ID: 648130

Licensing and Market Availability Plans

Currently in phase III trials

Summary

Risankizumab is in clinical development for moderate to severe ulcerative colitis. Ulcerative colitis is one of two major types of inflammatory bowel disease (IBD). It is a long-term immune-mediated inflammatory disorder where the colon and rectum become inflamed and small ulcers can develop on the colon's lining, which can cause symptoms such as rectal bleeding and recurring diarrhoea. The main aims of treatment are to reduce symptoms, known as inducing remission, and maintaining remission. Current ulcerative colitis treatment options have relatively low remission rates and/or are associated with loss of response over time and possible adverse side effects. In addition, despite the advent of novel treatments to control the disease, many patients still require a colectomy (surgical removal of all or part of the colon). Therefore, there is a significant unmet need to develop new medicinal products for ulcerative colitis that are more effective and are associated with fewer adverse effects.

Risankizumab is a man-made protein that acts like antibodies within the human immune system. It specifically binds to a particular cytokine (IL-23) and block its activity. IL-23 is involved in causing inflammation, therefore, blocking IL-23 reduces inflammation. If licensed, risankizumab will offer an additional treatment option for adult patients with moderate to severe ulcerative colitis.

Proposed Indication

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

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Treatment of moderately to severely active ulcerative colitis.¹

Technology

Description

Risankizumab (Skyrizi; BI-655066; ABBV066) is a humanised immunoglobulin G1 (IgG1) monoclonal antibody that selectively binds with high affinity to the p19 subunit of human interleukin (IL)- 23 cytokine without binding to IL-12 and inhibits its interaction with the IL-23 receptor complex.^{1,2} IL-23 is a cytokine that is involved in inflammatory and immune responses. By blocking IL-23 from binding to its receptor, risankizumab inhibits IL-23-dependent cell signalling and release of proinflammatory cytokines.² IL-23 plays a key part in the induction and function of immune cells, including T-helper 17 cells, innate lymphoid cells, $\gamma\delta$ T-cells, and natural killer cells, which are responsible for tissue inflammation, destruction, and aberrant tissue repair that underlies the pathology of several immune-related disorders, including ulcerative colitis.³

In phase III clinical trials (NCT03398148, NCT03398135), risankizumab is administered as an intravenous infusion or subcutaneous injection.¹

Key Innovation

Selective IL-23 inhibition, without concurrent inhibition of IL-12 has demonstrated superior clinical response in other diseases.⁴

Current treatment options for ulcerative colitis largely include 5-aminosalicylates, glucocorticoids, thiopurines, the Janus-associated kinase (JAK) inhibitor tofacitinib and biologics. Tumour necrosis factor (TNF) antagonists effectively induce and maintain disease remission, but up to one third of patients do not respond to induction treatment and approximately 40% of patients who initially benefited from this treatment lose response subsequently.^{5,6} Moreover, anti-TNF therapy is associated with potentially serious adverse effects, as TNF treatments target inflammation in general, whilst interleukin therapies target only the specific interleukin.^{5,7}

If licensed, risankizumab will offer an additional treatment option for patients, aged 16 and over, with moderate to severe ulcerative colitis.

Regulatory & Development Status

Risankizumab has Marketing Authorisation in the UK/EU for plaque psoriasis and psoriatic arthritis.²

Risankizumab is in phase III/II clinical development for:⁸

- Plaque psoriasis
- Psoriatic arthritis
- Palmoplantar pustulosis
- Crohn's Disease

Patient Group

Disease Area and Clinical Need

Ulcerative colitis is one of two major types of inflammatory bowel disease (IBD), the other condition being Crohn's disease.⁹ It is a long-term condition where the colon and rectum become inflamed and small ulcers

can develop on the colon's lining, which can bleed and produce pus. Some people may go for weeks or months with very mild symptoms, or none at all, known as remission, followed by periods where the symptoms are particularly troublesome, known as flare-ups or relapses.¹⁰ Symptoms of active disease or relapse include bloody diarrhoea, an urgent need to defecate, tiredness and abdominal pain.^{10,11} The exact cause of ulcerative colitis is unknown, although it is thought to be the result of a problem with the immune system. Many experts believe ulcerative colitis is the result of an autoimmune condition whereby the immune system mistakes bacteria in the colon which aids digestion, for a harmful infection. This causes the immune system to attack healthy tissue and leads to the colon and rectum becoming inflamed.¹² It is also believed that inherited genes are a factor in the development of ulcerative colitis, and certain environmental factors such as viral and bacterial infection, air pollution, medication and diet may be potential triggers.^{9,12}

Ulcerative colitis is the most common type of IBD.¹¹ It is estimated that ulcerative colitis affects about one in every 420 people in the UK and that around 146,000 people in England have ulcerative colitis, of whom about 52% have moderate to severe disease.^{13,14} 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.¹⁴ According to hospital episode statistics for England in 2020-21 there were a total of 109,967 finished consultant episodes (FCEs) where ulcerative colitis (ICD-10 code K51) was recorded as primary diagnosis, which resulted in 98,926 admissions and 88,128 day cases.¹⁵

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) currently recommends the following treatment options for moderate to severe ulcerative colitis:^{6,16,17}

- Tofacitinib
- Vedolizumab
- Infliximab, adalimumab, golimumab
- Filgotinib
- Ustekinumab

Clinical Trial Information

Trial	<p>M16-067; NCT03398148; 2016-004677-40; A Multicenter, Randomised, Double-Blind, Placebo Controlled Induction Study to Evaluate the Efficacy and Safety of Risankizumab in Subjects With Moderately to Severely Active Ulcerative Colitis</p> <p>Phase II/III – Active, not recruiting</p> <p>Locations: 20 EU countries, UK, USA, Canada and other countries</p> <p>Primary completion date: November 2022</p>
Trial Design	Randomised, parallel assignments, double blinded, placebo-controlled
Population	N=~1554 aged 16 to 80 years old; confirmed diagnosis of ulcerative colitis (UC) for at least 3 months prior to baseline.
Intervention(s)	<ul style="list-style-type: none"> • Risankizumab (dose 1, 2 or 3) intravenous infusion • Risankizumab (dose 2 or 3) SC
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome measure:

	<ul style="list-style-type: none"> Percentage of Participants with Clinical Remission per Adapted Mayo Score [Time Frame: Week 12] <p>See trial record for full list of other outcomes</p>
Results (efficacy)	-
Results (safety)	-

Trial	<p>M16-066; NCT03398135; 2016-004676-22; A Multicenter, Randomised, Double-Blind, Placebo Controlled 52-Week Maintenance and an Open-Label Extension Study of the Efficacy and Safety of Risankizumab in Subjects With Ulcerative Colitis</p> <p>Phase III - enrolling by invitation</p> <p>Locations: 20 EU countries, UK, USA, Canada and other countries</p> <p>Primary completion date: December 2023</p>
Trial Design	Randomised, parallel assignment, triple blinded, placebo-controlled
Population	N=~942; aged between 16 and 80 years old; participants who have completed Study M16-067 and have achieved clinical response as defined in the protocol
Intervention(s)	Risankizumab (dose 1 or 2) SC
Comparator(s)	Matched placebo
Outcome(s)	<p>Primary outcome measure:</p> <ul style="list-style-type: none"> Percentage of Participants with Clinical Remission per Adapted Mayo Score [Time Frame: Week 52] Percentage of Participants with Adverse Events (AE) [Time Frame: Up to Week 300] <p>See trial record for full list of other outcomes.</p>
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The list price of risankizumab is £3326.09.¹⁸

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Etrasimod for previously treated moderately to severely active ulcerative colitis (GID-TA10991). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Mirikizumab for previously treated moderately to severely active ulcerative colitis (GID-TA10872). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Etrolizumab for treating moderately to severely active ulcerative colitis (GID-TA10717). Expected date of issue to be confirmed.

- NICE technology appraisal in development. Upadacitinib for treating moderately to severely active ulcerative colitis (GID-TA10866). Expected January 2023.
- NICE technology appraisal in development. Ozanimod for treating moderately to severely active ulcerative colitis (GID-TA10732). Expected September 2022.
- NICE technology appraisal in development. Filgotinib for treating moderately to severely active ulcerative colitis (TA792). June 2022.
- NICE technology appraisal. Ustekinumab for treating moderately to severely active ulcerative colitis (TA633). June 2020.
- NICE technology appraisal. Tofacitinib for moderately to severely active ulcerative colitis (TA547). November 2018.
- NICE technology appraisal. Infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy (TA329). February 2015.
- NICE technology appraisal. Infliximab for acute exacerbations of ulcerative colitis (TA163). December 2008.
- NICE guideline. Ulcerative colitis: management (NG130). May 2019.
- NICE quality standard. Inflammatory bowel disease (QS81). February 2015.
- NICE evidence summary. Remsima (infliximab biosimilar) for subcutaneous injection for managing Crohn's disease and ulcerative colitis (ES35). February 2021.

NHS England (Policy/Commissioning) Guidance

- NHS England 2013/14. Standard Contract for Colorectal: Complex Inflammatory Bowel Disease (Adult). A08/S/c

Other Guidance

- European Crohn's and Colitis Organisation (ECCO). ECCO Guidelines on Therapeutics in Ulcerative Colitis: Medical Treatment. 2021.¹⁹
- NICE Clinical Knowledge Summary. Ulcerative Colitis. 2020.²⁰
- British Society of Gastroenterology. BSG consensus guidelines on the management of Inflammatory Bowel Disease in adults. 2019.²¹

Additional Information

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NB: This briefing presents independent research funded by the National Institute for Health and Care Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.