Health Technology Briefing
December 2022

Guselkumab for treating moderately to severely active Crohn's disease

Company/Developer	Janssen UK

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 24050	NICE ID: 10614	UKPS ID: 656225

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

Guselkumab is in clinical development for the treatment of moderately to severely active Crohn's disease. Crohn's disease is a lifelong condition where parts of the digestive system become inflamed causing painful ulcers and inflammation most commonly in the small intestine and colon. The main symptoms of Crohn's disease are diarrhoea, stomach aches and cramps, blood in stool, tiredness and weight loss. Symptoms often follow a pattern where individuals with the condition have periods of no symptoms or mild symptoms (remission) followed by periods where their symptoms are particularly troublesome (flare-ups or relapses). Treatments are available but there remains an unmet need for additional therapies that target new pathways that may offer greater efficacy and durable long-term disease control.

Guselkumab is a monoclonal antibody (a type of protein) which is designed to attach to interleukin 23 (IL-23) and block its activity. IL-23 is a messenger substance that controls the growth and maturation of some types of T cells. These T cells, which are part of the body's immune system (the body's natural defences), are involved in causing inflammation. By blocking the action of IL-23, guselkumab reduces inflammation and other symptoms of Crohn's disease. Guselkumab would be administered by subcutaneous injection. If licenced, guselkumab would provide an additional treatment option for adult patients with moderately to severely active Crohn's disease.

Proposed Indication

Moderately to severely active Crohn's disease.[1]

Technology

Description

Guselkumab (Tremfya) is a human IgG1λ monoclonal antibody (mAb) that binds selectively to the interleukin 23 (IL-23) protein with high specificity and affinity. IL-23, a regulatory cytokine, affects the differentiation, expansion, and survival of T cell subsets, (for example, Th17 cells and Tc17 cells) and innate immune cell subsets, which represent sources of effector cytokines, including IL-17A, IL-17F and IL-22 that drive inflammatory disease. In humans, selective blockade of IL-23 was shown to normalise production of these cytokines.[2]

Guselkumab is currently in clinical development for the treatment of moderately to severely active Crohn's disease. In the phase III clinical trial (GRAVITI, NCT05197049), patients will be administered guselkumab as a subcutaneous (SC) injection.[1]

Key Innovation

Conventional therapies including corticosteroids, thiopurines, and methotrexate have been used commonly as first-line therapies to treat Crohn's disease. However, these agents are often ineffective in maintaining clinical remission and have considerable toxicity. In addition, patients with refractory or more severe disease may not benefit sufficiently from conventional therapies and often need treatment with biologics. Currently, several biologics are available for the treatment of moderately to severely active Crohn's disease. Despite the increased effectiveness of biologics, many patients experience treatment failure, intolerance, and decreased efficacy over time. Therefore, a need remains for novel biologic therapies that target new pathways that may offer greater efficacy and durable long-term disease control for patients with Crohn's disease. In previous studies, guselkumab treatment resulted in improvements in clinical and endoscopic end points, and reduction in levels of inflammatory markers. There were improvements in patient-reported outcomes for patients with Crohn's disease whose health-related quality of life is often negatively affected by their disease.[3]

If licensed, guselkumab would provide an additional treatment option for patients with Crohn's disease.

Regulatory & Development Status

Guselkumab is currently licensed in the UK for the following indications:[2]

- Moderate to severe plaque psoriasis in adults who are candidates for systemic therapy
- Alone or in combination with methotrexate (MTX) for the treatment of active psoriatic arthritis in adult patients who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug (DMARD) therapy

Guselkumab is also in phase II and III clinical development for several indications, some of which include:[4]

- Pityriasis rubra pilaris
- Psoriatic arthritis
- Ulcerative colitis
- Giant cell arteritis
- Scalp psoriasis

Patient Group

Disease Area and Clinical Need

Crohn's disease is a lifelong condition where parts of the digestive system become inflamed. It is one type of a condition called inflammatory bowel disease (IBD).[5] In Crohn's disease, the immune system starts attacking the gut. This causes painful ulcers and inflammation and is most common in the small intestine and colon.[6] The exact cause of Crohn's disease is unknown. It is thought that several things could play a role, including genes, immune system problems, smoking, a previous stomach illness or an abnormal balance of gut bacteria.[5] Without treatment, symptoms of Crohn's disease can be constant or may come and go every few weeks or months. When the symptoms come back, it is called a flare-up or relapse. The periods between flare-ups are called remission. The main symptoms of Crohn's disease are diarrhoea, stomach aches and cramps, blood in stool, tiredness and weight loss.[7] When symptoms are present, it is described as active Crohn's disease.[6]

At least 1 in every 323 people in the UK are living with Crohn's disease.[6] The incidence of Crohn's disease in the UK is about 83 per million people per year, and the prevalence is 10.6 per 100,000 people in the UK.[8] In England (2021-22), there were 151,340 finished consultant episodes (FCEs) and 140,775 admissions for Crohn's disease (ICD-10 code K50) which resulted in 85,964 FCE bed days and 126,981 day cases.[9]

Recommended Treatment Options

Treatment is largely directed at the induction and maintenance of remission and the relief of symptoms. The aims of drug treatment are to reduce symptoms and maintain or improve quality of life, while minimising toxicity related to drugs over both the short and long term.[10] NICE recommends the following pharmacological treatment options for moderate to severe active Crohn's disease:[10]

- Infliximab or adalimumab for the treatment of severe, active Crohn's disease, following inadequate response to conventional therapies or in those who are intolerant of or have contra-indications to conventional therapy.[11]
- Vedolizumab or ustekinumab are recommended for moderately to severely active Crohn's disease when conventional therapy or therapy with adalimumab or infliximab is unsuccessful, is contra-indicated or not tolerated.[12,13]

Clinical Trial Information

Trial	**GRAVITI, NCT05197049, 2020-006165-11;** A Randomized, Double-blind, Placebo-controlled, Parallel-group, Multicenter Study to Evaluate the Efficacy and Safety of Guselkumab Subcutaneous Induction Therapy in Participants With Moderately to Severely Active Crohn's Disease **Phase III** – Recruiting **Locations:** 15 EU countries, UK, USA, Canada and other countries **Primary completion date:** July 2023
Trial Design	Randomised, parallel assignment, double-blind, placebo-controlled
Population	N=318 (estimated); Subjects with a diagnosis of Crohn's disease of at least 3 months in duration; have moderate to severe Crohn's disease, and demonstrated intolerance or inadequate response to conventional or to biologic therapy for Crohn's disease ; aged 18 years and older
Intervention(s)	Guselkumab SC (dose 1 and 2, or dose 1 and 3)

Comparator(s)	Matched placebo
Outcome(s)	Primary outcome measures: • Clinical remission at week 12 [time frame: week 12] • Endoscopic response at week 12 [time frame: week 12] See trial record for full list of other outcome measures
Results (efficacy)	-
Results (safety)	-

Clinical Trial Information	
Trial	**GALAXI, NCT03466411, 2017-002195-13;** A Phase 2/3, Randomized, Double-blind, Placebo- and Active-controlled, Parallel-group, Multicenter Protocol to Evaluate the Efficacy and Safety of Guselkumab in Participants With Moderately to Severely Active Crohn's Disease **Phase II/III** – Active, not recruiting **Locations:** 16 EU countries, UK, USA, Canada and other countries **Primary completion date:** April 2024
Trial Design	Randomised, parallel assignment, double-blind, placebo- and active-controlled
Population	N=1340 (estimated); Subjects with Crohn's disease or fistulizing Crohn's disease of at least 3 months duration; have moderate to severe Crohn's disease, and demonstrated intolerance or inadequate response to conventional or to biologic therapy for Crohn's disease; aged 18 years and older
Intervention(s)	Guselkumab IV and SC
Comparator(s)	Ustekinumab IV and SC, and placebo IV
Outcome(s)	Primary outcome measures: • Phase 2: change from baseline in the Crohn's disease activity index (CDAI) score at week 12 [time frame: baseline and week 12] • Phase 3: clinical response at week 12 and clinical remission at week 48 [time frame: baseline to week 48] • Phase 3: clinical response at week 12 and endoscopic response at week 48 [time frame: baseline to week 48] See trial record for full list of other outcome measures
Results (efficacy)	At week 12, significantly greater reductions in Crohn's Disease Activity Index from baseline (least squares means: 200 mg: –160.4, 600 mg: –138.9, and 1200 mg: –144.9 vs placebo: –36.2; all, $P < .05$) and significantly greater proportions of patients achieved clinical remission in each guselkumab group vs placebo (Crohn's Disease Activity Index <150; 57.4%, 55.6%, and 45.9% vs 16.4%; all, $P < .05$). Greater proportions of patients receiving guselkumab achieved clinical response, Patient Reported Outcomes-2

	remission, clinical-biomarker response, and endoscopic response at week 12 versus placebo. Efficacy of ustekinumab versus placebo was also demonstrated.[3]
Results (safety)	Safety event rates were generally similar across treatment groups.[3]

Estimated Cost

Guselkumab is already marketed in the UK for the treatment of plaque psoriasis and psoriatic arthritis; a 100mg/1ml solution for injection pre-filled pen costs £2,250.[14]

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Etrolizumab for previously treated moderately to severely active Crohn's disease (GID-TA10870). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Upadacitinib for previously treated moderately to severely active Crohn's disease (GID-TA10997). Expected June 2023.
- NICE technology appraisal in development. Risankizumab for previously treated moderately to severely active Crohn's disease (GID-TA10884). Expected March 2023.
- NICE technology appraisal. Ustekinumab for moderately to severely active Crohn's disease after previous treatment (TA456). July 2017.
- NICE technology appraisal. Vedolizumab for treating moderately to severely active Crohn's disease after prior therapy (TA352). August 2015.
- NICE technology appraisal. Infliximab and adalimumab for the treatment of Crohn's disease (TA187). May 2010.
- NICE guideline. Crohn's disease: management (NG129). May 2019.
- NICE quality standard. Inflammatory bowel disease (QS81). February 2015.
- NICE interventional procedures guidance. Extracorporeal photopheresis for Crohn's disease (IPG288). February 2009.
- NICE interventional procedures guidance. Leukapheresis for inflammatory bowel disease (IPG126). June 2005.

NHS England (Policy/Commissioning) Guidance

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

Other Guidance

- Torres J, Bonovas S, Doherty G, Kucharzik T, Gisbert JP, Raine T et al. ECCO Guidelines on Therapeutics in Crohn's Disease: Medical Treatment. 2019.[15]
- Lamb CA, Kennedy NA, Raine T, Hendy PA, Smith PJ, Limdi JK et al. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. 2019.[16]
- Lichtenstein GR, Loftus EV, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACG Clinical Guideline: Management of Crohn's Disease in Adults. 2018.[17]

Additional Information

References

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3 Sandborn WJ, D'Haens GR, Reinisch W, Panés J, Chan D, Gonzalez S, et al. Guselkumab for the Treatment of Crohn's Disease: Induction Results From the Phase 2 GALAXI-1 Study. *Gastroenterology*. 2022;162(6):1650-64.e8. Available from: https://doi.org/10.1053/j.gastro.2022.01.047.

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