Health Technology Briefing
October 2024

Vedolizumab for treating moderately to severely active ulcerative colitis in children aged 2 to 17 years

Company/Developer	Takeda UK Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 38149	NICE ID: Not Available	UKPS ID: 666529

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Vedolizumab is currently in clinical development for the treatment of moderately to severely active ulcerative colitis (UC) in children and teenagers (paediatric patients). UC, a type of inflammatory bowel disease, is a long-term condition where the colon and rectum become inflamed and small ulcers can develop on the colon's lining, which may bleed and produce pus. Symptoms of UC include recurring diarrhoea, which may contain blood, mucus or pus, stomach pain, the need to frequently empty the bowels, fatigue, loss of appetite and weight loss. The exact cause of UC is unknown, although it is thought to result from a problem with the immune system. There is a high unmet need for new safe and effective treatment options in UC in paediatric populations, especially new therapies that can provide improved long-term efficacy.

Vedolizumab is a human monoclonal antibody, which is a manufactured version of an immune protein created by the body to fight infection. It is given by intravenous (into the vein) infusion. Vedolizumab blocks immune cells from binding of cells in the gut, therefore stopping the action of the immune cell and potentially decreasing inflammation. If licensed, vedolizumab will offer an additional treatment option for paediatric patients with moderately to severely active UC.

Proposed Indication

For the treatment of children and teenagers with moderate to severe ulcerative colitis (UC).[1]

Technology

Description

Vedolizumab (Entyvio, MLN0002, Kynteles) is a humanised monoclonal antibody that binds specifically to the $\alpha_4\beta_7$ integrin, which inhibits the adhesion of gut homing T helper lymphocytes to mucosal adhesin cell adhesion molecule-1 (MAdCAM-1). MAdCAM-1 is mainly expressed on gut endothelial cells and plays a critical role in the homing of T lymphocytes to tissues within the gastrointestinal (GI) tract. The α4β7 integrin is expressed on a discrete subset of memory T helper lymphocytes which preferentially migrate into the GI tract and cause inflammation that is characteristic of UC. [1,2]

Vedolizumab is currently in clinical development for the treatment of moderately to severely active UC among patients aged 2-17 years old.[1] In the phase III clinical trial (NCT04779307), during the induction period participants will receive three doses of vedolizumab (between 150mg and 300mg based on weight at baseline) by intravenous (IV) infusion at day 1, week 2, and week 6. At week 14, participants who achieve clinical response will be randomly assigned high (150mg to 300mg) or low dose (100mg to 150mg) vedolizumab IV infusions every 8 weeks up to week 46 during the maintenance period.[1]

Key Innovation

Standard treatments for UC are steroids and biological therapies, but not all patients respond to these treatments.[3] Of the available biologics for adults, only infliximab and adalimumab are currently approved for children. However, approximately 15–20% of patients with inflammatory bowel disease (IBD) do not respond to these therapies and another 30–40% stop responding.[4] A multicentre, prospective cohort study which evaluated the effectiveness and safety of vedolizumab as induction therapy for children with IBD found an improvement in disease activity as early as week 6, with 42% of children with UC in steroid-free and exclusive enteral nutrition-free clinical remission at week 14 (exclusive enteral nutrition means all calories are received through a special nutrition formula and no regular food is eaten).[4,5] Since vedolizumab targets the immune system in the gut, rather than the whole body, it is likely to have a lower risk of serious infections than systemic immunosuppressants.[6]

If licensed, vedolizumab will offer an additional treatment option for paediatric patients with moderately to severely active UC.

Regulatory & Development Status

Vedolizumab currently has Marketing Authorisation in the EU/UK for the following indications:[7]

- treatment of adults with moderately to severely active UC who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a TNFα antagonist
- treatment of adults with moderately to severely active Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a TNFα antagonist
- treatment of adult patients with moderately to severely active chronic pouchitis, who have undergone proctocolectomy and ileal pouch anal anastomosis for UC, and have had an inadequate response with or lost response to antibiotic therapy

Vedolizumab is in phase III/II clinical development for the following indications:[8]

- Pouchitis
- Crohn's disease
- Collagenous gastritis
- Acute graft versus host disease

Patient Group

Disease Area and Clinical Need

UC is the most common type of IBD.[7] UC is more common in adults; however in children it predominately presents between the ages of 5 and 16 years.[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 either no or very mild symptoms, known as remission, followed by periods where the symptoms are particularly troublesome, known as flare-ups or relapses. Symptoms of UC include recurring diarrhoea, which may contain blood, mucus or pus, stomach pain, the need to frequently empty the bowels, fatigue, loss of appetite and weight loss.[7,10] The exact cause of UC is unknown, although it is thought to be the result of an autoimmune condition whereby the immune system mistakes "helpful" bacteria in the colon, which aid digestion, for a harmful infection. This causes the immune system to attack healthy tissue, which leads to the colon and rectum becoming inflamed.[11] It is also believed that genes are a factor in the development of UC, and certain environmental factors such as viral and bacterial infection, air pollution, medication and diet may be potential triggers.[11,12]

UC affects males and females at approximately equal rates. The incidence of paediatric-onset UC, which represents about 15–20% of all UC cases, ranges from 1–4 per 100,000 per year in most North American and European regions.[13] In England, 2022-23, when considering all patients and not specifically paediatrics, there were 139,419 finished consultant episodes (FCEs) and 127,198 admissions for UC (ICD-10 code K51) which resulted in 83,684 FCE bed days and 115,015 day cases.[14] When adjusted to represent the incidence of paediatric-onset UC (approximately 15-20% of all UC cases), these figures become 20,913-27,884 FCEs and 19,080-25,440 admissions for UC which resulted in 12,553-16,737 FCE bed days and 17,252-23,003 day cases.

Recommended Treatment Options

Treatment is focused on treating active disease to manage symptoms and to induce and maintain remission. The National Institute for Health and Care Excellence (NICE) recommends the following:[9]

- topical or oral aminosalicylates for acute mild-to-moderate UC
- topical or oral corticosteroid for children whom aminosalicylates are unsuitable in mild-to-moderate UC
- intravenous corticosteroids (e.g. hydrocortisone or methylprednisolone) in acute severe UC
- if intravenous corticosteroids show little or no improvement within 72 hours, children over 6 years can be provided with infliximab
- If the disease does not adequately respond to oral corticosteroids (beclometasone, budesonide, hydrocortisone, or prednisolone) then an immunosuppressant (such as mercaptopurine or azathioprine) may be considered.[15]

Clinical Trial Information

Trial	NCT04779307, **EudraCT** 2020-004300-34; A Randomized, Double-Blind, Phase 3 Study to Evaluate the Efficacy and Safety of Vedolizumab Intravenous as

	Maintenance Therapy in Pediatric Subjects With Moderately to Severely Active Ulcerative Colitis Who Achieved Clinical Response Following Open-Label Vedolizumab Intravenous Therapy **Phase III –** Active, not recruiting **Locations:** Seven EU countries, UK, USA, Canada and five other countries **Primary completion date:** August 2025
Trial Design	Randomised, parallel assignment, quadruple masking
Population	Estimated N=120; subjects with moderately to severely active UC, unresponsive or intolerant to their current standard of care; aged 2 to 17 years old.
Intervention(s)	Vedolizumab intravenous infusion (dose is dependent on participant's weight)
Comparator(s)	-
Outcome(s)	Primary outcome: percentage of participants with clinical remission at week 54 based on modified Mayo score. See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Vedolizumab is already marketed in the UK for Crohn's disease and UC. The NHS indicative cost of one 300mg powder for concentrate for solution for infusion vial is £2050.00.[16]

Relevant Guidance

NICE Guidance

- NICE technology appraisal. Etrasimod for treating moderately to severely active ulcerative colitis in people aged 16 and over (TA956). March 2024.
- 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 guideline. Ulcerative colitis: management (NG130). May 2019.
- NICE quality standard. Inflammatory bowel disease (QS81). February 2015.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract Paediatric Medicine: Gastroenterology, Hepatology and Nutrition. E03/S/c.
- NHS England 2013/14. Standard Contract for Colorectal: Complex Inflammatory Bowel Disease (Adult). A08/S/c.

Other Guidance

- NHS University Hospitals of Leicester. Management of acute severe ulcerative colitis in children. 2021.[17]

- European Crohn's and Colitis Organization and European Society of Paediatric Gastroenterology, Hepatology and Nutrition. Management of Paediatric Ulcerative Colitis, Part 1: Ambulatory Care-An Evidence-based Guideline. 2018.[18]
- Tun GS, Harris A, Lobo AJ. Ulcerative colitis: management in adults, children and young people – concise guidance. 2017.[19]
- Fell JM, Muhammed R, Spray C, Crook K, Russell RK. Management of ulcerative colitis. 2016.[20]

Additional Information

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3 National Health Service (NHS) Health Research Authority. *Efficacy and Safety of Vedolizumab in children with Ulcerative Colitis*. 2021. Available from: https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/efficacy-and-safety-of-vedolizumab-in-children-with-ulcerative-colitis/ [Accessed 29 August 2024].

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