



AWTTC

All Wales Therapeutics & Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

Vedolizumab (Entyvio®) for the treatment of inflammatory bowel disease in children and young people aged 6 to 17 years: for ulcerative colitis following loss of response or non-response to anti-TNF treatment; for Crohn's disease following loss of response or non-response to anti-TNF treatment and ustekinumab (OW24)

February 2023

ONE WALES INTERIM DECISION

Vedolizumab (Entyvio®) for the treatment of inflammatory bowel disease in children and young people aged 6 to 17 years: for ulcerative colitis following loss of response or non-response to anti-TNF treatment; for Crohn's disease following loss of response or non-response to anti-TNF treatment and ustekinumab

Date of advice: February 2023

The following One Wales Medicines Assessment Group (OWMAG) recommendation has been endorsed by health board Chief Executives.

Using the starting and stopping criteria, vedolizumab (Entyvio®) can be made available within NHS Wales for the treatment of inflammatory bowel disease in children and young people aged 6 to 17 years: for ulcerative colitis following loss of response or non-response to anti-TNF treatment; for Crohn's disease following loss of response or non-response to anti-TNF treatment and ustekinumab.

The risks and benefits of the off-label use of vedolizumab (Entyvio®) for this indication should be clearly stated and discussed with the patient to allow informed consent.

Providers should consult the relevant guidelines on prescribing unlicensed medicines before any off-label medicines are prescribed.

This advice will be reviewed after 12 months or earlier if new evidence becomes available.

Clinician responsibility

Clinicians will be obliged to collect and monitor patient outcomes. Evidence of clinical outcomes will be taken into consideration when reviewing the One Wales Medicines Assessment Group decision.

Health board responsibility

Health boards will take responsibility for implementing One Wales Medicines Assessment Group decisions and ensuring that a process is in place for monitoring clinical outcomes.

One Wales advice promotes consistency of access across NHS Wales.

Starting and stopping criteria for vedolizumab (Entyvio®) for the treatment of inflammatory bowel disease in children and young people aged 6 to 17 years: for ulcerative colitis following loss of response or non-response to anti-TNF treatment; for Crohn's disease following loss of response or non-response to anti-TNF treatment and ustekinumab

Starting criteria

Patients aged 6 to 17 years with ulcerative colitis following loss of response or non-response to anti-TNF inhibitors or when anti-TNF inhibitors cannot be tolerated or are contraindicated.

Patients aged 6 to 17 years with Crohn's disease following loss of response or non-response to anti-TNF inhibitors and ustekinumab or when anti-TNF inhibitors and ustekinumab cannot be tolerated or are contraindicated.

Screening

Prescribers should be aware of the potential increased risk of opportunistic infections or infections for which the gut is a defensive barrier; vedolizumab treatment is not to be initiated in patients with active, severe infections until the infections are controlled. Patients must be screened for active tuberculosis (TB) before commencing treatment; vedolizumab is contraindicated in patients with active TB and those with latent TB given appropriate anti-TB therapy before beginning vedolizumab¹. There is a theoretical risk of progressive multifocal leukoencephalopathy (PML). Patients should receive a patient information leaflet and a Patient Alert Card.

Dose

In patients weighing ≥ 30 kg, 300 mg of vedolizumab should be given intravenously over 30 minutes on weeks zero, two and six and then every 8 weeks thereafter. No specific guidelines exist for paediatric dosing. Younger paediatric patients may require an individualised dose of 6 mg/kg up to a maximum of 300 mg, or a body surface area-based dose (considering a standard adult of 1.73 m^2)². A suggested dosage regimen is:

Child's weight	Dose to be prescribed
10 to 15kg	150mg
15 to 30kg	200mg
≥ 30 kg	300mg

Response to vedolizumab can take time (≥ 16 weeks)². Patients who have not shown a sufficient response or who have experienced a decrease in their response may benefit from an increase in dosing frequency up to every four weeks, according to clinical judgement.

Outcome data, including dosing frequency and duration of treatment, should be collected to inform future policy changes.

Monitoring

- Infusion-related reactions and hypersensitivity reactions including anaphylactic shock
- New onset or worsening of neurological signs indicative of progressive multifocal leukoencephalopathy (PML).
- Routine blood tests including FBC, U&E, LFTs, CRP and ESR at induction and 6-monthly thereafter.
- Extra blood tests including vitamins D and B12, folate and ferritin after 6 months of treatment and 6-monthly thereafter.
- Endoscopy (annual)
- Treatment response indicators at induction and 6-monthly thereafter
 - Faecal calprotectin levels
 - Mucosal or endoscopic healing
 - Patient height and weight
 - Paediatric Crohn's Disease Activity Index or Paediatric Ulcerative Colitis Activity Index scores (or appropriate scoring measurements used in clinical practice)

Stopping criteria

- Treatment failure, progression of symptoms or minimal response, including need for surgery
- Toxicity to treatment (that cannot or does not respond to temporary treatment interruption)
- Patient request

Outcome data, including reasons for stopping treatment, should be collected to inform future policy changes.

Continuation of treatment

- At 12 months, patients should be reassessed to determine whether treatment should continue. Treatment should only continue if there is clear evidence of ongoing clinical benefit.
- For patients in complete remission at 12 months, consider stopping vedolizumab, resuming treatment if there is a relapse.
- Patients who continue vedolizumab should be reassessed at least every 12 months to decide whether continued treatment is justified.

References

1. Takeda UK Ltd. Entyvio® 300 mg powder for concentrate for solution for infusion. March 2022. Available at: <https://www.medicines.org.uk/emc/product/5442/smpc#INDICATIONS>. Accessed December 2022.
2. van Rheenen PF, Aloi M, Assa A et al. The Medical Management of Paediatric Crohn's Disease: an ECCO-ESPGHAN Guideline Update. Journal of Crohn's and Colitis. 2021;15(2):171-194. Accessed January 2023.

Prepared by the All Wales Therapeutics and Toxicology Centre

One Wales Medicines Assessment Group summary of decision rationale

Medicine: **vedolizumab (Entyvio®)**

Indication: **For the treatment of inflammatory bowel disease in children and young people aged 6 to 17 years: for ulcerative colitis following loss of response or non-response to anti-TNF treatment; for Crohn's disease following loss of response or non-response to anti-TNF treatment and ustekinumab**

Meeting date: **19 December 2022**

Criteria	OWMAG opinion
Indication	<p>After discussion, OWMAG agreed that the age range of children and young people (CYP) with IBD eligible to receive treatment with vedolizumab should be defined in the indication to those aged 6 to 17 years. This is to align with the licensed indication for the use of anti-TNF inhibitors for UC and CD in the paediatric population. IPFR remains a route of access for children under 6 years.</p>
Clinical effectiveness	<p>OWMAG notes that the main clinical effectiveness evidence is from a phase II, randomised, dose-ranging study and a systematic review that identified ten studies. The data is limited but suggests remission rates for both ulcerative colitis and Crohn's disease are comparable if not better than those seen in adults. However, results are subject to uncertainty given that there is a lack of placebo-controlled studies in CYP at this time although four phase III clinical trials in the paediatric population are currently underway.</p> <p>The positive reports from experts who had used vedolizumab to treat CYP with IBD were noted most particularly, the resultant reduction in rates of surgery. Many CYP have more aggressive forms of the disease and need earlier intervention with biologics.</p> <p>OWMAG considers that the evidence provided demonstrated clinical effectiveness.</p>
Cost-effectiveness	<p>There is no cost-effectiveness evidence in CYPs. However, OWMAG noted that vedolizumab was considered to be cost-effective by NICE for the treatment of adults with ulcerative colitis and Crohn's disease although the relevance of these cost-effectiveness studies to the paediatric population is uncertain.</p> <p>OWMAG acknowledge that disease presentation is usually severe in CYP and there is a large associated cost to the NHS of managing both UC and CD in children and adolescents, most especially as surgery is often required after current licensed treatments have failed to control the disease. Additionally, CYP often need psychological support following surgery. It was also noted that the</p>

	<p>treatment of flares is associated with a significant cost burden to the NHS. OWMAG considers it likely that, taking these factors into account, vedolizumab would also be a cost-effective treatment for CYP as for adults.</p>
Budget impact	<p>OWMAG considers the estimate of patient numbers to be reasonable. The group acknowledges that budget impact estimates are subject to uncertainty due to lack of longer-term discontinuation rate data making it difficult to estimate the proportion of CYP discontinuing treatment throughout the 3-year timeframe.</p> <p>The Clinical experts indicated that the number of CYP being diagnosed is increasing based on better diagnostic monitoring. It was noted by one of the clinical experts that patients will transition in to adult services which would affect patient numbers. This treatment is approved by NICE in adults.</p> <p>OWMAG acknowledges the budget impact is likely to be lower for year one than estimated given that half of patients are already receiving treatment through IPFR. OWMAG also acknowledges that the overall budget impact may be lower than predicted as some patients may be eligible to receive vedolizumab as part of an imminent clinical trial.</p> <p>OWMAG considers that the base case provided in the report is a reasonable estimate of the associated cost to NHS Wales.</p>
Other factors	<p>OWMAG acknowledges that paediatric patients with IBD which is poorly controlled are at risk of complications and repeated surgical interventions.</p> <p>OWMAG acknowledges the significant burden IBD has on patients' health and health-related quality of life, and how the symptoms of CD and UC, and their unpredictable nature, can be detrimental to both the physical and mental health of CYPs and negatively impact on educational attainment, future work and career choices, and social and emotional interactions and relationships.</p> <p>OWMAG acknowledges that there is an unmet medical need for CYPs who have failed conventional treatments in the pathway, there is no alternative licensed therapy and patients may be dependent on steroids or have to undergo surgery at a formative time in their lives to control the disease. Vedolizumab may offer an effective treatment option for these patients with the potential to prevent or delay surgery.</p>
Final recommendation	<p>OWMAG recommends the use of vedolizumab (Entyvio®) for the treatment of inflammatory bowel disease in children</p>

	<p>and young people aged 6 to 17 years: for ulcerative colitis following loss of response or non-response to anti-TNF treatment; for Crohn's disease following loss of response or non-response to anti-TNF treatment and ustekinumab.</p> <p>This recommendation is subject to the development of appropriate start/stop criteria.</p>
Summary of rationale	<p>There is some limited clinical evidence to support vedolizumab as an effective and relatively safe option for the treatment of inflammatory bowel disease in children and young people aged 6 to 17 years: for ulcerative colitis following loss of response or non-response to anti-TNF treatment; for Crohn's disease following loss of response or non-response to anti-TNF treatment and ustekinumab. OWMAG are of the opinion that, as there is no evidence to the contrary, it is reasonable to assume that the efficacy and safety of vedolizumab in CYP from 6 years of age would be similar to that seen in adults.</p> <p>Paediatric patients with IBD which is poorly controlled are at risk of complications and repeated surgical interventions. IBD places a significant burden on both a CYP's physical and mental health and their overall quality of life at this formative time. There are no licensed alternative treatment options and access to vedolizumab for this indication may offer an effective treatment option for these patients and potentially avoid reliance on corticosteroids and/or prevent or delay surgery to control the disease.</p> <p>A proportion of the patient population in Wales are already receiving this treatment via Individual Patient Funding Request, supporting the use on an All Wales basis would ensure equity of access and prevent unnecessary delay.</p>

The information in this document is intended to help healthcare providers make an informed decision. This document should not be used as a substitute for professional medical advice. Care has been taken to ensure the information is accurate and complete at the time of publication. However, the All Wales Therapeutics and Toxicology Centre (AWTTC) do not make any guarantees to that effect. The information in this document is subject to review and may be updated or withdrawn at any time. AWTTC accept no liability in association with the use of its content. An Equality and Health Impact Assessment (EHIA) has been completed in relation to the One Wales policy and this found there to be a positive impact. Key actions have been identified and these can be found in the [One Wales Policy EHIA document](#).

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