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)

May 2024

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 original advice: February 2023
Date of review: April 2024

The following One Wales Medicines Assessment Group (OWMAG) recommendation has been noted by the All Wales Medicines Strategy Group (AWMSG) and ratified by Welsh Government

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 3 years 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 vedolizumab[1]. 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
≥30kg	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 April 2024.
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 April 2024.

First Review of One Wales Decision – April 2024

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)

This report was prepared by the All Wales Therapeutics and Toxicology Centre in March 2024. It summarises any new evidence available and patient outcome data collected since the One Wales decision in March 2023.

Background: Ulcerative colitis (UC) and Crohn's disease (CD) are the two main forms of inflammatory bowel disease (IBD). They are lifelong, chronic conditions that follow an unpredictable relapsing and remitting course and can cause significant morbidity. IBD negatively affects the quality of life of children and adolescents based on its impact on the physical, emotional and social wellbeing of these patients, especially if poorly controlled.

Clinicians in Wales consider there is an unmet need and have identified a cohort of people who could benefit from this treatment. This includes children and young people (CYP) aged 6 to 17 years who have failed current treatments in the pathway and where there is no alternative licensed therapy to meet their needs. These patients may be dependent on steroids to control the disease and would be at risk of complications and repeated surgical interventions if their inflammatory bowel disease is poorly controlled. This medicine was therefore considered suitable for assessment via the One Wales process.

Current One Wales Decision: Supported

Licence status: Off-label use for this licensed medicine. [Confidential information removed].

Guidelines: There have been no relevant updates to existing guidelines identified.

Licensed alternative medicines or Health Technology Assessment advice for alternative medicines: No new medicines or Health Technology Assessment advice reported.

Effectiveness:

Patel et al (2024) conduced a retrospective comparative effectiveness study of second-line ustekinumab and vedolizumab therapies in paediatric patients with UC who failed anti-TNF therapy. Results for the vedolizumab arm are relevant as this treatment is recommended by One Wales as a second line treatment option for the treatment of paediatric UC. Of the 262 patients included in the vedolizumab cohort, 28.3% achieved corticosteroid-free clinical remission (defined as a Paediatric Ulcerative Colitis Activity Index (PUCAI) < 10 or a physician global assessment (PGA) = 1) at 6-month follow up. Clinical response was achieved in 39.7% of 232 patients assessed for this secondary endpoint. Satisfactory nutritional and growth

status was achieved in 82.7% and 89.7% of children receiving vedolizumab, respectively. Around one-third (32%) of children stopped treatment with vedolizumab by the end of year one. Infection rates were low and no malignancies were reported.

Safety: No relevant safety analyses were identified in the review literature search. Outcome data provided by the tertiary specialist centre in Cardiff reported [confidential information removed].

Cost-effectiveness: No relevant cost-effectiveness analyses were identified in the repeat literature search.

Budget impact: In the original evidence summary it was estimated that 22 patients in Wales start treatment each year with all assumed to have at least 12 months of treatment. Twenty-three patients have received treatment with vedolizumab over the last 12 months in Wales; 21 at the tertiary centre in Cardiff and Vale UHB and [confidential data removed]. Of these, 10 commenced treatment prior to the availability of vedolizumab through the One Wales decision in March 2023; treatment before this would have been initiated following agreement through the Individual Patient Funding Request (IPFR) process. The number of actual patients who received treatment over the past 12 months is consistent with that estimated for the original assessment.

Impact on health and social care services: Minimal.

Patient outcome data: Outcome data have been provided for twenty-five patients which includes [confidential data removed]. Eighteen have been treated for UC, five for CD and [confidential data removed]. Twelve patients currently receiving treatment remain on an 8-weekly dosing schedule with nine receiving treatment every 4-6 weeks; two patients are due to start treatment. [Confidential data removed]. The discontinuation rate is lower than the estimated rates used in the original submission, no data on discontinuation rates in paediatrics were found. No other clinical data have been provided.

Evaluation of evidence

No significant new evidence has been published which challenges the current One Wales advice. The number of children on treatment is in accordance with the budget impact estimates used in the evidence summary report and treatment is being tolerated. AWTTC recommends continuing access in Wales to vedolizumab 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.

Next review date: April 2027

References: a full reference list is available on request.

This document includes evidence published since the last review or full assessment of this medicine for the indication under consideration. It does not replace the original full evidence status report. Any previous reviews and the original full evidence status report are available on request by email to AWTTC@wales.nhs.uk.

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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