



AWTTC

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

One Wales Medicines Assessment Group Recommendation: Vedolizumab (Entyvio®) for the treatment of immune checkpoint inhibitor induced grade 2-4 enterocolitis (OW22)

September 2024

ONE WALES MEDICINES ASSESSMENT GROUP (OWMAG)

Vedolizumab (Entyvio®) for the treatment of immune checkpoint inhibitor induced grade 2-4 enterocolitis

Date of advice: September 2024

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

Using the agreed starting and stopping criteria vedolizumab can be made available within NHS Wales:

- for the treatment of immune checkpoint inhibitor (ICI) induced grade 3-4 enterocolitis, where symptoms have not responded to first line immunosuppression with corticosteroids and infliximab or when infliximab is unsuitable
- for the treatment of ICI-induced grade 3–4 enterocolitis in patients who are corticosteroid-dependent requiring multiple challenges with corticosteroids when symptoms have not responded to infliximab or when infliximab is unsuitable
- as an option for the treatment of ICI-induced grade 2 enterocolitis, where symptoms have not responded to first line immunosuppression with corticosteroids or in patients who are corticosteroid-dependent requiring multiple challenges with corticosteroids

The risks and benefits of the off-label use of vedolizumab for these indications 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 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 assists consistency of access across NHS Wales.

Starting and stopping criteria for vedolizumab: for the treatment of immune checkpoint inhibitor (ICI) induced grade 3-4 enterocolitis, where symptoms have not responded to first line immunosuppression with corticosteroids and infliximab or when infliximab is unsuitable; for the treatment of ICI-induced grade 3–4 enterocolitis in patients who are corticosteroid-dependent requiring multiple challenges with corticosteroids when symptoms have not responded to infliximab or when infliximab is unsuitable; as an option for the treatment of ICI-induced grade 2 enterocolitis, where symptoms have not responded to first line immunosuppression with corticosteroids or who are corticosteroid-dependent requiring multiple challenges with corticosteroids

Developed in collaboration with clinicians in Wales.

Starting criteria

Patients with moderate to severe or life threatening (grade 2-4) diarrhoea or colitis with any of the following symptoms/features present:

- 4 or more stools/day over baseline
- Severe abdominal pain
- Fever
- Dehydration
- Blood or mucus in stool
- Flexible sigmoidoscopy indicates presence of high-risk endoscopic features, mucosal ulceration or extensive colitis
- Colostomy patients

And symptoms are persisting for three or more days despite high dose methylprednisolone (1-2 mg/kg/day) (grade 3-4 disease) or five or more days despite oral prednisolone 40-60 mg/day (grade 2 disease). Or oral prednisolone dose cannot be tapered to 10 mg/day or less without re-flare of symptoms.

And symptoms are persisting despite infliximab 5-10 mg/kg given for up to three doses, or where infliximab is deemed unsuitable (due to high tumour burden, patient age, patient frailty or a contra-indication to the use of infliximab - see One Wales guidance for infliximab). Vedolizumab may be considered as an option for grade 2 disease in those patients not responding to corticosteroids but clinicians should consider the additional cost of vedolizumab when compared to infliximab and weigh this against any additional perceived benefits before starting treatment. Infliximab should be the first option for patients with more severe disease (grade 3-4).

Screening

Prior to commencing vedolizumab, pre-screening should be undertaken to exclude:

- Active or latent tuberculosis
- Hepatitis virus or HIV
- Current acute infections (viral, bacterial, fungal or parasitic)
- Gastrointestinal perforation

In cases of life-threatening toxicity, consider risk/benefit if screening could result in significant delay to treatment.

Dose

The recommended treatment dose regimen for vedolizumab is 300 mg given intravenously on weeks zero, two and six. Not all cases will require three doses, treatment can be stopped before completing the course if there is sufficient response after the first or second dose. Standard treatment though is 3 doses.

Only one course (three doses) may be issued in accordance with this advice. Requests for repeat courses or continuing treatment beyond three doses should be explored through funding mechanisms such as the individual patient funding request process.

Outcome data

The following should be collected to inform future policy changes:

- Patient numbers
- Number of doses received by the patient
- Grade of disease at start of treatment
- Prior enterocolitis treatments before starting vedolizumab
- Enterocolitis response to treatment with vedolizumab
- Ability to restart immunotherapy after treatment with vedolizumab
- Time from decision to treatment administration with vedolizumab.

Monitoring

- Infusion-related reactions including anaphylactic shock
- Injection site for signs of phlebitis
- Any new onset or worsening of neurological signs and symptoms
- Daily stool chart
- Daily bloods e.g., FBC, U&E, LFTs, CRP
- Blood cultures if pyrexial
- National Early Warning Score (NEWS) assessment
- Fluid balance
- Faecal calprotectin

Prescribers should consult the relevant Summary of Product Characteristics (SmPC) for any additional monitoring requirements and potential adverse effects. There is a potential risk of progressive multifocal leukoencephalopathy (PML). Patients should receive a patient information leaflet and a Patient Alert Card.

Stopping criteria

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

Failure to respond to vedolizumab

If there is no response or symptoms are deteriorating after one, two or three doses of vedolizumab then seek advice from Gastroenterology and/or consultant leads from the Immunotherapy toxicity service.

Reference

Merck Sharp Dohme. Vedolizumab (Entyvio) 300 mg powder for concentrate for solution for infusion. Available at: <https://www.medicines.org.uk/emc/product/5442/smpc>. Accessed 22 August 2024