Grŵp Strategaeth Meddyginiaethau Cymru Gyfan
All Wales Medicines Strategy Group

One Wales Medicines Assessment Group Recommendation
Infliximab powder for concentrate for solution for infusion (OW21)

Date of advice: September 2024
Date of last review: March 2026
AWTTC reference number: OW21

Using the agreed starting and stopping criteria infliximab can be made available within NHS Wales for the treatment of:

- immune checkpoint inhibitor (ICI) induced grade 2-4 enterocolitis, where symptoms have not responded to first line immunosuppression with corticosteroids
- ICI-induced grade 2–4 enterocolitis in patients who are corticosteroid-dependent requiring multiple challenges with corticosteroids
- ICI-induced grade 2-4 enterocolitis in patients requiring dose escalation to 10 mg/kg when there has been an inadequate response to standard 5 mg/kg dosing

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

The choice of infliximab product prescribed should be based on the acquisition cost and in accordance with the One Wales advice on use of biosimilars.

This recommendation has been endorsed by the All Wales Medicines Strategy Group (AWMSG) and ratified by Welsh Government.

This advice will be reviewed after 2 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 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 infliximab: for the treatment of immune checkpoint inhibitor (ICI) induced grade 2-4 enterocolitis, where symptoms have not responded to first line immunosuppression with corticosteroids; ICI-induced grade 2–4 enterocolitis in patients who are corticosteroid-dependent requiring multiple challenges with corticosteroids; ICI-induced grade 2-4 enterocolitis in patients requiring dose escalation to 10 mg/kg when there has been an inadequate response to standard 5 mg/kg dosing.

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 (1-2mg/kg/day) (Grade 3-4 disease) or five or more days despite oral prednisolone 40-60mg/day (Grade 2 disease). Or oral prednisolone dose cannot be tapered to 10mg/day or less without re-flare of symptoms.

Screening

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

- Active or latent tuberculosis
- Hepatitis virus or HIV
- Current acute infections (viral, bacterial, fungal or parasitic)
- Moderate to severe heart failure (NYHA class III/IV)
- Gastrointestinal perforation

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

Patients with high tumour disease burden, those who are frail or elderly or where there is a contra-indication to the use of infliximab should be discussed with gastroenterology and reviewed by Immunotherapy toxicity service and consideration given to using an alternative treatment option, which may include vedolizumab. This will be (see One Wales advice for vedolizumab)

Dose

The recommended treatment dose regimen for infliximab is 5 mg/kg by intravenous infusion on weeks zero, two and six. Some cases may require a shorter interval than 2 weeks between doses, specialist advice should be sought from the immunotherapy multidisciplinary team (MDT) or gastroenterology team. 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 however standard treatment is 3 doses. The dose may be escalated to 10 mg/kg in those patients who have shown an inadequate response to 5 mg/kg. For patients with low albumin (30g/L or less), the recommended dose is 10 mg/kg.

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.

The infliximab product available at the lowest acquisition cost should be prescribed.

Once infliximab has been given switch to oral prednisolone and wean as per local steroid taper guidelines.

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 infliximab
- Enterocolitis response to treatment with infliximab
- Ability to restart immunotherapy after treatment with infliximab
- Time from decision to treatment administration with infliximab.

Monitoring

- Infusion-related reactions including anaphylactic shock
- Injection site for signs of phlebitis
- 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.

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

For patients who develop hepatotoxicity during treatment (alanine aminotransferase [ALT] increases or aspartate aminotransferase [AST] increases at or above 5 times the upper limit of normal), treatment should be discontinued.

Failure to respond to infliximab

If there is no response or symptoms are deteriorating after one, two or three doses of infliximab, or following dose escalation, then consider switching to vedolizumab with advice from Gastroenterology and/or consultant leads from Immunotherapy toxicity service.

Reference

Merck Sharp Dohme. Infliximab (Remicade) 100 mg powder for concentrate for solution for infusion. Available at: https://www.medicines.org.uk/emc/product/3831/smpc. Accessed March 2026

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

First Review of One Wales Decision – December 2025

Infliximab to treat immune checkpoint inhibitor (ICI)-induced grade 2–4 enterocolitis that has not responded to first-line immunosuppression with corticosteroids, including patients who are corticosteroid-dependent and need multiple challenges with corticosteroids, and patients who need a higher dose of 10 mg/kg infliximab because symptoms have not responded to 5 mg/kg infliximab (OW21)

This report was prepared by the All Wales Therapeutics and Toxicology Centre in December 2025. It summarises any new evidence available and patient outcome data collected since the One Wales decision in September 2024.

Background: Immune checkpoint inhibitors (ICIs) are a recent advancement in cancer immunotherapy. They negatively target regulators of the immune response which results in immune system activation and anti-tumour immunity. This specific immune system activation can potentially affect any organ system at the same time, most commonly the skin, gut, liver and endocrine system. Immune-related enterocolitis is one of the most common and severe immune-related adverse events associated with ICI treatment.

For moderate and severe (grade 2–4) ICI-induced enterocolitis, corticosteroids are the standard frontline treatment. Grade 2–4 ICI-induced enterocolitis that has not responded to corticosteroids is currently treated off-licence in Wales with infliximab, after clinicians in Wales submitted it for consideration through the One Wales process. They considered there was an unmet need in Wales and identified a cohort of patients who could benefit from this treatment.

Current One Wales Decision: supported for use

Licence status: off-label use for this licensed medicine

Guidelines: British Society of Gastroenterology (BSG) practice guidance on the management of acute and chronic gastrointestinal symptoms and complications as a result of treatment for cancer was published in 2025. The guidance states that for grade 3 and 4 diarrhoea (and grade 2 diarrhoea that does not respond to oral prednisolone) patients should be admitted to hospital and started on intravenous methylprednisolone 1 mg/kg daily. If there is endoscopic evidence of enterocolitis and still no response to corticosteroids within 2–3 days, second-line treatment with infliximab (5–10 mg/kg) or vedolizumab should be started and expert advice sought. The guidance states that infliximab and vedolizumab are equally efficacious.

No relevant updates to other guidelines were identified.

Licensed alternative medicines or health technology assessment (HTA) advice for alternative medicines: no new medicines or HTA advice reported.

Effectiveness: AWTTC conducted a literature search in November 2025 to find new evidence for the use of infliximab to treat ICI-induced enterocolitis. The search excluded: articles published before 2024; articles that reviewed evidence previously presented in AWTTC's first Evidence Summary Report; case reports; and conference abstracts. Two studies were identified: a systematic review of the efficacy of infliximab compared with vedolizumab to treat ICI-induced enterocolitis, and a retrospective cohort study of 1,151 patients who developed ICI-induced enterocolitis. Both studies are discussed below.

A systematic review and meta-analysis of the efficacy of infliximab versus vedolizumab in the treatment of ICI-induced enterocolitis (Shambhavi et al. (2025) identified six retrospective cohort studies with 645 patients in total.

The results showed that patients treated with vedolizumab had lower rates of recurrence of enterocolitis compared with patients given infliximab (odds ratio [OR]: 0.29; 95% confidence interval [CI]: 0.15, 0.54). The analysis also showed that vedolizumab was associated with a lesser duration of steroid exposure when compared to infliximab (mean difference: −16.88 days, 95% CI: −20.47, −13.30). However, while vedolizumab showed improved remission, there was no statistically significant difference in remission rates between vedolizumab and infliximab monotherapy (OR: 3.16, 95% CI: 0.29, 34.01). It is worth noting that this analysis included patients for whom infliximab treatment failed and who went on to receive vedolizumab, which may have skewed the results. Overall, the mean number of doses needed to achieve remission were lower for infliximab than for vedolizumab (mean difference:1.16, 95% CI: 0.09, 2.22).

A limitation of this study is that it analysed only observational studies, which might have influenced the effect size. Although the pooled overall OR for remission showed a favourable profile for vedolizumab over infliximab, it was statistically insignificant due to the small sample size. The pooled studies did show low heterogeneity for recurrence and steroid exposure duration but considerable heterogeneity for remission and number of doses needed to achieve remission. The authors suggest that the evidence supports the superiority of vedolizumab over infliximab as a maintenance treatment for ICI-induced enterocolitis.

A single-centre retrospective study (Shatila et al. (2025) included 1,151 patients (675 males, aged 55–72 years) who developed confirmed ICI-induced enterocolitis. Of 1,151 patients, 841 patients (73.0%) were treated with corticosteroids, and 384 patients (33.3%) needed treatment with intravenous corticosteroids; 534 patients (46.4%) needed additional immunosuppressive therapy.

Outcomes of ICI-induced enterocolitis were compared between 182 patients given infliximab (159 with grade 2 or higher diarrhoea and 102 with grade 2 or higher colitis) and 265 patients given vedolizumab (217 with grade 2 or higher diarrhoea and 110 with grade 2 or higher colitis). Patients treated with infliximab tended to have more severe enterocolitis.

The median time between onset of ICI-induced enterocolitis and administration of additional immunosuppressive therapy was significantly different between

treatments: 14 days (range 7–43 days) for infliximab compared with 33 days (15–60 days) for vedolizumab (P<0.001). The median time between administration and improvement of symptoms was only 4.5 days (range 2–22.7 days) for infliximab compared with 30 days (14–65 days) for vedolizumab (P<0.0001). The median number of doses given was lower for infliximab: two (range one–two doses) compared with three (two–four doses) for vedolizumab (P<0.0001). The median duration of ICI-induced enterocolitis symptoms was shorter for infliximab: 24.5 days (range 12–67 days) compared with 56 days (range 21–108 days) for vedolizumab (P<0.001). There were no significant differences between infliximab and vedolizumab in terms of duration of steroid treatment (33 vs 31 days), hospitalisation rates (71.8% vs 64.2%), clinical improvement or remission (91.8% vs 95.1%) or endoscopic remission (72.4% vs 79.3%).

The authors concluded that infliximab and vedolizumab appeared equally efficacious in achieving clinical symptom remission in ICI-induced enterocolitis. However, infliximab may offer a slight advantage in reducing overall symptom duration.

Safety: No new safety issues or relevant safety analyses were identified in the repeat literature search.

In their systematic review, Shambhavi et al. reported that only two of the six included studies reported infection data, so a quantitative analysis of safety data could not be performed; one of these studies reported lower rates of infection with vedolizumab than with infliximab.

[Confidential information removed].

Ongoing studies: A phase I/II trial NCT04407247, comparing infliximab with vedolizumab to treat grade 2 or higher ICI-related enterocolitis, is ongoing and expected to complete by end 2027.

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

Budget impact: Clinicians from south-east Wales and north Wales reported that they have given infliximab to a total of 20 patients with ICI-induced enterocolitis in the 17 months between September 2024 and January 2026. This compares to a predicted 12 patients per year with one of these patients receiving the higher dose of 10 mg/kg infliximab. Extrapolating patient numbers to consider patients from south-west Wales, would give an estimated 25 patients over 17 months, which is 50% higher than originally estimated. However, 40% of patients received less than three doses and taking both these factors into account, the budget impact is expected to be slightly higher than that predicted in the original assessment.

Impact on health and social care services: Minimal.

Patient outcome data: Clinicians in south-east and north Wales reported outcome data for 18 patients [confidential information removed].

Evaluation of evidence

No significant new evidence has been published that challenges the previous evidence presented. Extrapolating patient numbers for Wales based on those given for two of the three Welsh cancer treatment centres, would indicate that patient numbers are about 50% higher than those originally predicted; taking into account that 40% of patients received less than three doses of infliximab, the budget impact may reasonably be assumed to be slightly higher than that originally estimated. However, this increase is offset by the lower than predicted use of vedolizumab for this patient population (see the OW22 review report for further detail). Based on available outcome data, infliximab appears to be an effective treatment option for most patients who have received it, with 89% of patients reporting either a full (56%) or partial (33%) resolution of symptoms where an outcome was reported. AWTTC recommends continuing access to infliximab in NHS Wales through the One Wales Medicines process for the treatment of ICI-induced enterocolitis as per the recommendation.

Next review date: March 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 the AWTTC website. 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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