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

One Wales Medicines Assessment Group Recommendation:
Infliximab for the treatment of immune checkpoint inhibitor induced grade 2-4 enterocolitis (OW21)

September 2024

ONE WALES MEDICINES ASSESSMENT GROUP (OWMAG)

Infliximab 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 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

Infliximab should be prescribed on the basis of lowest acquisition cost.

The risks and benefits of the off-label use of infliximab 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 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 22 August 2024