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

Infliximab for the treatment of refractory pulmonary sarcoidosis that has not responded to corticosteroids and other immunosuppressants (OW23)

May 2024

ONE WALES INTERIM DECISION

Infliximab for the treatment of refractory pulmonary sarcoidosis that has not responded to corticosteroids and other immunosuppressants

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 agreed starting and stopping criteria, infliximab can be made available within NHS Wales for the treatment of refractory pulmonary sarcoidosis that has not responded to corticosteroids and other immunosupressants.

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

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.

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 infliximab for the treatment of refractory pulmonary sarcoidosis that has not responded to corticosteroids and other immunosuppressants

Developed in collaboration with the South Wales Interstitial Lung Disease multi-disciplinary team and clinicians in North Wales.

Starting criteria:

If disease modifying drugs are required in pulmonary sarcoidosis corticosteroids in the form of prednisolone is the usual first line of therapy. Second-line therapies include hydroxychloroquine, methotrexate, azathioprine, mycophenolate, leflunomide and rarely cyclophosphamide. These are initiated for a variety of reasons including:

- Disease progression or ongoing symptomatic burden despite corticosteroids
- Corticosteroid contraindication (intolerable side effect burden, co-morbidities, patient choice)
- Inability to wean prednisolone below 10 mg/day

If a patient has an intolerable side effect burden or evidence of disease progression despite one of the second line therapies an alternative second line therapy is trialled. Third-line biological agents (infliximab) are only considered in pulmonary sarcoidosis when there is failure of, a contraindication to, or intolerance of, second line therapies. This decision would be made at either the South Wales or North Wales Interstitial Lung Disease multi-disciplinary team meetings.

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)
- pregnancy.

Prescribers should consult the relevant Summary of Product Characteristics (SmPC) for other cautions to treatment.

Dose

For pulmonary sarcoidosis the usual starting dose is 3 mg/kg at Weeks 0, 2, 6 and then every 8 weeks afterwards. If necessary the dose may be increased on consultant decision to 5 mg/kg if only a minimal improvement has been observed by the fourth dose. Maintenance treatment might continue for 1 year or 2 years.

The administration of infliximab should be in accordance with the SmPC including the use of any premedications and monitoring requirements.

Concomitant administration with an immunosuppressant is recommended, this is usually the immunosuppressant the patient is currently taking, to reduce the risk of them developing antibodies to infliximab, which are associated with an increased frequency of infusion reactions.

Outcome data, including the dosing regimen should be collected to inform future policy changes.

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

Monitoring

- Blood tests e.g., FBC, U&E, LFTs, CRP as part of the intial screening and prior to infusion
- Infusion-related reactions including anaphylactic shock
- Injection site for signs of phlebitis

Prescribers should consult the relevant SmPC for any other monitoring requirements and potential adverse effects. The patient should be given the information leaflet and special Alert Card, which will be supplied with the infliximab.
Outcome measures should include: improvement in symptoms, improvement or stabilisation of pulmonary function (forced vital capacity and imaging), quality of life and possible reduction in oral corticosteroid dose.

Stopping criteria:

- No response at 6 months*
- Progression of symptoms
- 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.
*The patient's response to therapy is assessed after 6 months and if the patient has not responded to treatment, infliximab will be discontinued.

References:

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 15 May 2024

Royal Brompton & Harefield NHS Foundation Trust. Guidelines for the use of infliximab in adult patients with sarcoidosis. Oct 2018.

Thillai M, Atkins CP, Crawshaw A et al. BTS Clinical Statement on pulmonary sarcoidosis. Thorax. 2021;76:4-20.

First Review of One Wales Decision – April 2024

Infliximab for the treatment of refractory pulmonary sarcoidosis that has not responded to corticosteroids and other immunosuppressants (OW23)

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 interim decision in March 2023.

Background: Sarcoidosis is a rare condition that causes small patches of swollen tissue (called granulomas) to develop in the body. Sarcoidosis can affect any organ in the body although most patients (90%) will have lung involvement, also known as 'pulmonary sarcoidosis'.

There is currently no cure for sarcoidosis. Clinicians in Wales considered there to be an unmet need in NHS Wales and identified a cohort of patients who could benefit from infliximab treatment. In Wales, refractory pulmonary sarcoidosis that has not responded to treatment with corticosteroids or other immunosuppressants is treated with add-on infliximab through the One Wales process. The recommended dose of infliximab is 3 mg/kg, with the option to escalate to 5 mg/kg if clinically indicated, given as an intravenous infusion at Weeks 0, 2 and 6, followed by maintenance doses every 8 weeks.

In November 2023, NHS England published a Clinical Commissioning Policy recommending the off-label use of infliximab (5 mg/kg dose) to treat refractory sarcoidosis (excluding neurosarcoidosis) that has not responded to standard treatments or where standard treatments are unsuitable. Infliximab for refractory or progressive neurosarcoidosis has been available through a Clinical Commissioning Policy since 2020.

Current One Wales Decision: Supported

Licence status: Infliximab is not currently licensed to treat refractory pulmonary sarcoidosis that not has not responded to corticosteroids and other immunosuppressants; its use in this indication is off-label. AWTTC is not aware of any plans to pursue marketing authorisation of infliximab for this indication at this time.

Guidelines: No new guidelines or relevant updates to existing guidelines have been identified.

Licensed alternative medicines or Health Technology Assessment advice for alternative medicines: No new treatments have been licensed for this indication.

Effectiveness: A literature search by AWTTC identified no new relevant studies or meta-analyses.

Safety: No relevant safety analyses were identified in the review literature search.

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

Budget impact: Clinical experts report that [confidential data removed] have started treatment with infliximab for refractory pulmonary sarcoidosis since March 2023. This is [confidential data removed] than our original estimate that six patients per year would be started on infliximab.

Impact on health and social care services: Minimal.

Patient outcome data: A small number of patients are receiving infliximab for pulmonary sarcoidosis in Wales. Patient outcome data suggests that patients have experienced increases in quality of life and improvement of their symptoms.

Evaluation of evidence

No new clinical evidence has been published that would change the original One Wales recommendation, and no new treatment guidelines have been published. Data from clinicians in Wales show that patient numbers are lower than the original budget impact estimates, and where outcomes are available, infliximab treatment has resulted in improvement in symptoms and in quality of life. AWTTC recommends that it would be appropriate to retain access to infliximab for the treatment of refractory pulmonary sarcoidosis **that has not responded to corticosteroids and other immunosuppressants.**

Next review date: May 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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