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

Evidence Status Report: infliximab for the treatment of grade 3–4 steroid-refractory pneumonitis induced by immune checkpoint inhibitor (ICI) therapy **(OW34)**

Report prepared by the All Wales Therapeutics and Toxicology Centre
December 2025

Key findings

Licence status
Infliximab is not licensed for treating grade 3–4 steroid-refractory pneumonitis induced by immune checkpoint inhibitor (ICI) therapy; its use for this indication is off-label.

Clinical evidence
Evidence comes from two systematic reviews, and retrospective case series and case reports. No randomised controlled trials of infliximab in the treatment of ICI-induced pneumonitis were identified. Overall, the evidence for the use of infliximab from the case reports and case series is mixed and inconclusive, and of very low quality.

Safety
No new safety signals have been observed for infliximab in this indication.

Patient factors
Patients would receive the first dose of infliximab in hospital. Infliximab is administered by intravenous infusion over a two-hour period. Due to risk of acute infusion-related reactions, patients should be monitored during and for at least one to two hours post-infusion.

Cost effectiveness
No cost-effectiveness evidence was identified for this use of infliximab, and in the absence of any clinical studies of infliximab for this indication, no cost-effectiveness analyses have been undertaken.

Budget impact
The additional use of infliximab is estimated to increase the annual spend associated with this patient group in Wales by [commercial in confidence figure removed] assuming no displacement of the very low cost comparator treatment, mycophenolate mofetil.

Impact on health and social care services
Minimal – due to the severity of the condition, patients with grade 3 or grade 4 ICI-induced pneumonitis will already be admitted to hospital with extensive monitoring. The addition of infliximab to the treatment pathway is likely to have a low additional impact.

Innovation and/or advantages
Infliximab offers an additional treatment option for some patients in this group. Clinicians in Wales suggest that the specificity of the immunosuppressive activity of infliximab might offer an advantage over other immunosuppressive agents with a broader spectrum of activity which may be detrimental to the ongoing control of the cancer targeted by ICI treatment.

Background

Clinicians in Wales consider there is an unmet need for treatment of grade 3–4 steroid-refractory pneumonitis induced by immune checkpoint inhibitor (ICI) therapy. They have identified a cohort of patients who might benefit from infliximab treatment. Infliximab was considered suitable for assessment though the One Wales medicines process following agreement by the AWMSG Scrutiny Panel.

The All Wales Therapeutics and Toxicology Centre (AWTTC) sought opinions from clinical experts in Wales. Clinical experts expressed a need for a clear treatment strategy or clinical guideline to manage ICI-induced pneumonitis in Wales. A small number of patients with steroid-refractory ICI-induced pneumonitis in Wales have received infliximab (off-label) through local agreements. A One Wales decision would ensure equity of access to infliximab across the country to treat steroid-refractory ICI-induced pneumonitis.

Target group

The indication considered is the treatment of steroid-refractory grade 3–4 pneumonitis induced by immune checkpoint inhibitors.

Marketing authorisation date: Not applicable, off-label

Infliximab is not licensed for the treatment of steroid-refractory grade 3–4 pneumonitis induced by ICIs. There are no plans to license infliximab for the indication under consideration.

Dosing information

The dose proposed by clinicians in Wales is 5 mg/kg by intravenous infusion over a 2-hour period at Week 0. This dose is the recommended infliximab dose for the majority of licensed indications[1]. Patients should be observed for at least 1–2 hours post-infusion for acute infusion-related reactions. A second, and third dose may be given, 2 and 6 weeks later. In some cases, a shorter interval may be required between doses and specialist advice should be sought from the immunotherapy team. This is the same dosing regimen as for the treatment of ICI-induced enterocolitis (OW21) and myocarditis (OW31).

Clinical background

Immune checkpoint inhibitor (ICI) therapy is a type of immunotherapy for several different types of cancer, including lung cancer and melanoma. Checkpoint proteins, such as PD-L1, CTLA-4 and PD-1, stop the immune system from attacking cancer cells; checkpoint inhibitors block these proteins and turn the immune system back on, to find and attack cancer cells[2]. However, ICIs can overstimulate the immune system,

leading to various side effects known as immune-related adverse events (irAEs) that can occur in any organ[3].

ICI-induced pneumonitis is an uncommon but potentially serious toxicity[4]. Presenting symptoms include dyspnoea, new or worsening cough, chest pain, fever and hypoxia. The diagnosis of ICI-induced pneumonitis can be challenging due to pre-existing inflammatory lung disease, chronic obstructive pulmonary disease, infections or concomitant treatment related pneumonitis that may occur with chemotherapy, targeted drugs and radiotherapy. If ICI-induced pneumonitis is suspected, a high resolution chest computed tomography (CT) scan and full clinical work-up is recommended to confirm diagnosis[5].

The severity of immune-related adverse events, including ICI-induced pneumonitis, is graded according to the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE) tool[6].

- Grade 3 pneumonitis – severe symptoms; oxygen indicated; limiting self-care activity of daily living.
- Grade 4 pneumonitis – life-threatening respiratory compromise; urgent intervention indicated (e.g. tracheotomy or intubation).

Time to onset of ICI-induced pneumonitis ranges from 9 days to 19.2 months, but in general, the median time to onset is approximately 2.5 months for monotherapy but earlier for anti-PD-L1/anti-CTLA-4 combination therapy[5]. While ICI-related pneumonitis is a rare event, it is frequently serious with up to one-third of patients presenting with events of grade 3 or higher, and a fatal outcome in up to 12% of patients[7].

Incidence

The incidence of any grade ICI-induced-pneumonitis in clinical studies is about 4% for anti-PD-1 therapies, 2% for anti-PD-L1 inhibitors and <1% for anti-CTLA-4 inhibitors; the incidence of high-grade pneumonitis is about 1%[5]. It is more frequent with anti-PD-L1/anti-CTLA-4 combination therapy versus monotherapy (10% versus 1%-5%, respectively)[5].

The National Immunotherapy Toxicity Sub-Group estimate that approximately 12 patients with steroid-resistant grade 3–4 ICI-induced pneumonitis across Wales would be eligible for treatment with infliximab each year.

Current treatment options and relevant guidance

The European Society for Medical Oncology (ESMO) guideline for the management of toxicities from immunotherapies recommends that first-line treatment for pneumonitis of grade 3 and above is with intravenous methylprednisolone at 1–2 mg/kg/day followed by steroid tapering over 6 to 8 weeks if respiratory symptoms improve[5]. For patients who have not responded to intravenous steroids within 72 hours, the addition of either infliximab (5 mg/kg, one dose, every two weeks if needed), tocilizumab (8 mg/kg, one dose, every two weeks if needed) or intravenous immunoglobulin (IVIG) (2 g/kg over 2–5 days) is recommended. Other options, such as mycophenolate mofetil (MMF) (1 g twice daily) or cyclophosphamide can be considered after individual assessment on a case-by-case basis. Additionally, the ESMO guidelines state that if symptoms are life-threatening, first-line therapy with

tocilizumab or infliximab, in addition to intravenous corticosteroids, is advocated as soon as possible[5].

The American Society of Clinical Oncology (ASCO) recommend that if no improvement is noted within 48 hours of high-dose steroid treatment, additional immunosuppression with either infliximab (5 mg/kg), MMF, IVIG or cyclophosphamide should be offered[4]. The Society for Immunotherapy of Cancer (SITC) Toxicity Management Working Group guidelines recommend a similar treatment pathway although also include tocilizumab as a second-line immunosuppressant option[8]. The US National Comprehensive Cancer Network (NCCN) guideline recommends treatment with either IVIG or MMF is used in preference to tocilizumab or infliximab due to the increased risk of gastrointestinal perforation with tocilizumab and data for infliximab showing a mixed response for treatment of ICI-induced pneumonitis[9]. It is also stated that MMF is unlikely to improve steroid-unresponsive pneumonitis immediately but may have clinical benefit to avoid steroid dependence[10]. Most guidelines also recommend empiric antibiotics in case of infection.

All guidelines highlight that recommendations for all second-line immunosuppression options are based on low quality evidence.

The NHS Wales National Immunotherapy Toxicity Sub-Group is currently developing an all-Wales consensus guideline on the management of ICI-induced toxicities including pneumonitis. Infliximab is their preferred second-line immunosuppressive therapy option for patients who are not at significant risk of autoimmune infections due to familiarity of use for other ICI-induced toxicities, there is some evidence for its effectiveness and there is less concern about its effect on ongoing cancer control than with some other alternative treatments. For older patients who may be more immunosuppressed, tocilizumab would be used in preference to infliximab as it is less immunosuppressive than infliximab. The National Immunotherapy Toxicity Sub-Group states that the treatment and management of this toxicity is complex and currently sub-optimal and routine early access to infliximab and tocilizumab may improve patient outcomes.

Clinicians from [confidential information removed].

Both ESMO and ASCO guidelines recommend that ICI treatment is permanently discontinued for pneumonitis of grade 3 and above[4,5]. However, the consensus recommendations from the US SITC Toxicity Management Working Group state that ICI rechallenge may be considered on a case-by-case basis for grade 3 pneumonitis but only if symptoms and imaging abnormalities resolve[8].

Summary of evidence on clinical effectiveness

AWTTC conducted a literature search during 19–24 September 2025 to look for evidence about the use of infliximab to treat steroid-refractory ICI-induced pneumonitis.

Database searches were performed using MEDLINE, EMBASE and the Cochrane Library. Search terms were: infliximab, renflexis, remicade, remsima, inflectra, zessly, flixabi; pneumonitis, pneumonia, (pneumoniti* or lung inflammation* or pulmonary inflammation*), immune checkpoint inhibitors, immune checkpoint inhibit* (immune adj2 checkpoint adj2 (inhibit* or blockade*)), ((ICI or ICIs) adj2 pneumonitis).

The primary outcomes of interest were symptom improvement or resolution in randomised controlled trials, systematic reviews, network meta-analyses, guidelines, case series, case reports, conference abstracts, retrospective studies, health-related quality of life, economic evaluations and adverse events. No date restrictions were applied; results were restricted to English language. Targeted searches of Google and Google Scholar were also performed. Conference abstracts and letters were included. Clinical authors at AWTTC sifted and screened the results of the clinical searches, and health economics authors sifted and screened the results of the searches for economic evaluations and quality of life. See the PRISMA diagram in Appendix 1.

A total of 394 clinical papers were retrieved during the literature search, from which 20 duplicates were removed. 374 clinical papers were screened by inspecting titles only, and 140 papers were screened by inspecting abstract and full text. Twenty-five papers were identified for inclusion in this report; one paper identified from the Google Scholar search was also included.

The literature search identified no clinical trials of infliximab in steroid-refractory ICI-induced pneumonitis; only systematic reviews, case reports and case series were identified.

In this evidence summary report, we include: two systematic reviews, four case series (15 patients), and 18 case reports or case series where only a single patient was identified (18 patients). We excluded reviews in which all the cases they reported were covered in other reviews; we also excluded case series and case reports that were covered in the two systematic reviews. The included case reports and cohort studies are listed in Appendix 2.

Efficacy

The two systematic reviews searched PubMed (Daetwyler et al. 2024) and Medline, Embase and Cochrane databases (Canadian Agency for Drugs and Technologies in Health (CADTH) 2024). Both reviews were broader searches for treatment of all types of immune therapy-related adverse events (Daetwyler et al. 2024), and for infliximab to treat immune ICI-related toxicities (CADTH 2024).

Corticosteroid-resistant immune-related adverse events: a systematic review (Daetwyler et al. 2024)

This systematic review summarises the available evidence for the treatment recommendations of ICI-induced toxicities including pneumonitis[7]. The review identified six case reports and seven case series with 50 patients treated with infliximab and also reviewed evidence for the use of other immunosuppressive agents, including IVIG, MMF, cyclophosphamide and tocilizumab for pneumonitis.

Most evidence was available for infliximab although results were mixed. For example, low success rates in the range of 25–33% were reported in three retrospective studies. Contrastingly, two retrospective studies indicated negative responses following infliximab treatment. Higher success rates were reported for alternative immunosuppressant treatments but based on less evidence. The fatality rate for patients with steroid-resistant pneumonitis, regardless of which additional suppressive treatment was chosen, was high at 67–100%.

The authors recommended that IVIG, and MMF should be used for steroid-resistant pneumonitis followed by tocilizumab if these fail. However, the treatment recommendations made in this systematic review rely heavily on single case reports and small case series which provide low level evidence and so may be subject to considerable uncertainty. The authors conclude that treatment decisions should be made on an individual basis, taking into consideration all clinical factors, drug availability, and local experience favouring one agent over another[7].

Infliximab for Immune Checkpoint Inhibitor Therapy-Related Toxicities (CADTH 2024)

CADTH published a rapid review summarising the evidence available for the use of infliximab as treatment for ICI therapy-related toxicities in June 2024, which included ICI-induced pneumonitis[3]. This review included case reports and case series identified in an earlier systematic review by Daetwyler et al. 2024 plus additional relevant publications.

In total, 18 studies were included; nine case reports and nine cases series giving a total of 74 patients reviewed. Combined analysis of the results from the systematic review and additional studies showed that the complete response rate of infliximab for the treatment of ICI-induced pneumonitis was 28.4%, with 1.4% of patients achieving a partial response and 70.2% showing no response. CADTH concluded that the mixed evidence available meant that the effectiveness of infliximab for the treatment of ICI-induced pneumonitis remains to be determined as prospective evidence is not yet available but that the use of infliximab for the treatment of pneumonitis is an option[3].

Case reports

Eighteen cases are listed in Table 2 in Appendix 2, two of which reported other ICI-induced toxicities in addition to pneumonitis[11,12].

The dose of infliximab was specified in ten cases and was most commonly 5 mg/kg (eight cases)[11,13-19]. When reported, patients mostly received one dose (eight cases) with two patients receiving two doses[14,19].

For the 16 cases where only pneumonitis was present, infliximab treatment led to improvement of pneumonitis symptoms in nine cases[14,15,17,18,20-24]. In seven cases infliximab treatment failed to improve pneumonitis[13,16,19,25-28] and in two of these cases, patients were given additional immunosuppressants after infliximab[19,26]. For the two cases with multiple toxicities, infliximab treatment led to improvement of pneumonitis in both cases[11,12].

Case series

Sun et al. (2025) reported four patients failed to show any improvement in their pneumonitis. Two of these patients required further treatment with additional immunosuppressants after receiving infliximab and one other patient died of cancer progression[29]. Tan et al. (2023) reported two patients who recovered from ICI-induced pneumonitis and had > 1 year survival from symptom onset. However, one patient failed to improve and died of pneumonitis[30]. Frost et al. (2023) reported six patients with worsening symptoms who failed to show any improvement after treatment with infliximab[31]. Sheshadri et al. (2022) also reported two patients who failed to improve with infliximab and died[32].

Safety
The SmPC lists very common (occurring in ≥ 1 in 10 people) adverse reactions as: viral infection (e.g. influenza, herpes virus infection), headache, upper respiratory tract infection, sinusitis, abdominal pain, nausea, infusion-related reaction and pain[1]. The most serious adverse drug reactions associated with the use of TNF blockers that have been reported for infliximab include hepatitis B virus reactivation, congestive heart failure, and serious infections (including sepsis, opportunistic infections and tuberculosis)[1].

Patients receiving infliximab must be monitored closely for infections before, during and after treatment, with monitoring continuing up to six months after infliximab was last given. Particular attention regarding infection risk should be paid when treating elderly populations. The SmPC's special warnings include details about infliximab's association with acute infusion-related events including anaphylactic shock and delayed hypersensitivity reactions. Infliximab is contra-indicated in patients with moderate or severe heart failure (NYHA class III/IV)[1] Patients should be closely monitored, and infliximab must not be continued in patients who develop new or worsening symptoms of heart failure.

One case report was identified of a patient who presented with hepatitis which was attributed to ICI-related toxicity and hepatotoxic adverse effects of infliximab[33]. Deaths due to infectious complications from use of infliximab in addition to corticosteroids were reported in some of the cases. However adverse events were inconsistently reported across most of the case reports and series. Clinicians in Wales reported [confidential information removed].

Experience of using infliximab in NHS Wales
Clinicians from [confidential information removed].

Discussion
Infliximab is listed as an option for the treatment of steroid-refractory ICI-induced pneumonitis in a number of international guidelines. However, all guidelines highlight that recommendations for all second-line immunosuppression treatment options are based on low-quality evidence.

In this evidence summary, we identified an additional 33 patients from the published literature not included in the two systematic reviews and two patients from NHS Wales who have received infliximab to treat ICI-induced pneumonitis. Of these 35 patients, 15 had a response to treatment with infliximab, 20 had no improvement and five were given additional immunosuppressants after infliximab. Of the 15 patients who responded to infliximab, four later died; two due to cancer progression; one due to multiple organ failure with an *Aspergillus* infection and one due to sepsis, likely developing after extended periods of steroid treatment.

The systematic reviews identified have included different case reports although there are some reports that are common to both reviews. The systematic reviews conclude that the evidence for the use of infliximab to treat steroid-refractory ICI-induced pneumonitis is mixed and inconclusive. This conclusion is further supported by the results of the additional cases we have identified where, overall, the evidence for the use of infliximab is mixed, and of very low quality. It is also not clear how many patients had grade 3 or 4 pneumonitis.

There are no clinical studies that evaluated the efficacy of infliximab to treat ICI-induced pneumonitis. Evidence is only available from case reports and case series, and systematic narrative reviews of case reports and case series; overall patient numbers remain low. Case reports are generally the lowest grade of evidence. It is difficult to compare cases; cases may not be generalisable. The amount of information given about each case varies; dose and outcome data vary. In some cases, it is not clear when infliximab was given (if the case was steroid-refractory). Patients often had complex diagnoses, some with multiple immune-related toxicities, and treatment rarely followed clinical guidelines in terms of escalation of additional immunosuppression treatments after inadequate response to first-line steroids.

Although the grade of pneumonitis was not stated in many studies, nearly all case reports are for patients where pneumonitis symptoms were severe. Many patients were treated with a number of immunosuppressive agents in addition to steroids and so the relative benefit of infliximab is difficult to ascertain. The concomitant use of immunosuppressive agents may be expected to have a compounding effect on suppressing the immune system; a number of patients developed infections, some proving fatal, which may have been attributable to this effect.

Patient organisation submission
We received a submission from the patient organisation Melanoma Focus, commenting on our assessment of infliximab to treat steroid-resistant ICI-induced pneumonitis. The main points of the submission are listed below.

- There is a growing population of melanoma patients who are younger in age; in the 15–44 years age group, melanoma is the second most common form of cancer in males and the third most common cancer in females.
- Checkpoint inhibitors, alone or in combination, are standard of care for all patients with metastatic melanoma and for high-risk stage II and III melanoma.
- Patients will generally accept significant toxicities to live longer. For metastatic melanoma, the longer-term survival rate is better for those treated with combination treatment. Therefore, patients, if fit enough, will likely be treated with combination therapy at the expense of approximately 60% of patients reporting grade 3–4 toxicities.
- ICIs have revolutionised melanoma care; 50% of patients treated with metastatic disease are now alive at 10 years. However, life-threatening (grade 3–4) toxicities are reported in 50–60% of patients on combination ICI therapy, and in about 20% of patients on single agent ICI therapy.
- Pulmonary inflammation (pneumonitis) is an increasingly recognised complication of ICI therapy occurring in around 6.6% of treated patients. The most severe toxicity can occur in 2% of patients and its incidence is rising every year.
- Pneumonitis is potentially fatal and early assessment and intervention are key. Standard guidelines for grade 3–4 toxicity recommend initial, high-dose corticosteroid treatment. Patients with pneumonitis often need additional immunosuppression with additional medicines, some of which target different chemicals released as part of the inflammatory process associated with checkpoint inhibitors and include infliximab, tocilizumab and abatacept.
- Melanoma Focus strongly supports the co-creation of guidelines for worsening or refractory pneumonitis under the guidance of respiratory medicine and/or medical oncologist. As patients with this condition can deteriorate rapidly, patients and emergency departments need to be aware to swiftly report

symptoms which may suggest possible pneumonitis and that it should be treated appropriately to avoid unnecessary long-term complications or death.

Ongoing clinical studies
No clinical studies are currently progressing for infliximab in this indication. An open-label randomised trial (study NCT04438382) using infliximab or IVIG for the treatment of steroid-refractory pneumonitis (grade 2 or higher) started in 2021, but terminated in 2023 due to difficulties in enrolling patients[34].

Cost-effectiveness evidence

No cost-effectiveness evidence was identified for this use of infliximab, and in the absence of any clinical studies of infliximab for this indication, no cost-effectiveness analyses have been undertaken.

Budget impact

Infliximab procurement costs are informed by a confidential NHS Wales contract price with a unit cost of a 100 mg vial ranging between [commercial in confidence figures removed] for the various biosimilars on all-Wales contract. NHS Wales prescribing figures from 2024 for infliximab 100 mg are used to calculate a weighted average procurement cost. The weighted average cost per 100 mg vial is [commercial in confidence figure removed] excluding VAT.

The average patient weight is calculated using population averages with an equal percentage of male and females. The recommended dose of 5 mg/kg for an average patient weight of 79 kg results in 4 vials per dose[35]. There is an assumption of no vial sharing; wastage is applied. The total infliximab procurement cost for a single dose is [commercial in confidence figure removed] excluding VAT.

The administration cost for the delivery of infliximab is sourced from the NHS reference costs 2023/24 with cost code SB12Z used for the first administration and SB15Z for additional delivery[36]. The first administration cost is £418. Delivery of subsequent dose is costed at £426. Based on clinical expert opinion, it is assumed patients receive three doses of infliximab at 5 mg/kg, the cost of which is [commercial in confidence figure removed] per patient excluding VAT.

Clinicians in Wales indicate that currently patients with steroid-refractory ICI-induced pneumonitis are predominantly treated with MMF. A typical regimen for MMF is 500 mg twice daily for 3 days increasing to between 1 – 1.5 g twice daily depending on response. Treatment with MMF is continued until the patient has been weaned off steroids and is stable; this is usually between 8-12 weeks after initiation of treatment.

MMF procurement costs are informed by confidential NHS Wales contract prices. The unit cost of MMF for 50 x 500 mg tablets ranges from [commercial in confidence figures removed] excluding VAT. Using the second lowest price of [commercial in confidence figure removed], the maximum acquisition cost of 1.5 mg MMF twice daily for 12 weeks is calculated as [commercial in confidence figure removed].

The National Immunotherapy Toxicity Sub-Group estimate that approximately 12 patients with steroid-resistant grade 3-4 ICI-induced pneumonitis across Wales would be eligible for treatment with infliximab each year.

Table 1. Estimated annual net cost for infliximab in comparison to MMF in Wales

	Per patient	For 12 patients
Medicine acquisition and administration costs		
Infliximab (3 doses)	¶¶	¶¶
MMF (1.5 mg twice daily for 12 weeks)	¶¶	¶¶
Assuming full displacement of MMF	¶¶	¶¶
MMF: mycophenolate mofetil ¶¶: commercial in confidence figure removed		

The introduction of infliximab for the indication under consideration will increase the spend for this patient group. Based on an estimated uptake of 12 patients receiving three doses of 5 mg/kg infliximab, the annual cost of infliximab will be [commercial in confidence figure removed] (excluding VAT). The degree of displacement of the comparator treatment MMF is difficult to estimate as some patients may still receive it alongside infliximab to support steroid taper. However, the low cost of 1.5 mg MMF twice daily for 12 weeks per patient will not significantly affect the overall budget impact; if all patients remain on MMF in addition to receiving treatment with infliximab, the total treatment cost for 12 patients is estimated to be [commercial in confidence figure removed].

Budget impact issues

- Infliximab biosimilar NHS Wales contract costs have been used in the calculations; costs may be higher for non-contracted products.
- Costs of additional screening and monitoring for bacterial, viral and fungal infections and adverse event costs are excluded from the budget impact both for infliximab and for comparator treatments.
- Clinical experts suggest that infliximab may result in better clinical outcomes for some patients and avoid the need for additional further treatments and shorten hospital stay.
- The lack of comparative data between treatments means that any additional benefit from infliximab cannot be quantified and taken into account in budget impact calculations.
- The budget impact calculations assume that all patients will receive the maximum 3 doses of infliximab; clinicians in Wales state that this is the usual intention although this is not achieved or required in all cases. Therefore, the budget impact may be overestimated.
- Administration costs for oral treatments (i.e. MMF) are assumed to be zero but may be associated with administration costs. However, these are expected to be minimal in comparison to administration costs associated with infliximab which is delivered by intravenous infusion.
- Medicine acquisition costs may be subject to VAT which has not been included in budget impact calculations.
- The use of ICIs is growing, and it is anticipated that patient numbers will increase over the next few years, which will have an additional budgetary impact in Wales.

Equality and health impact assessment

AWTTC have completed an Equality and Health Impact Assessment in parallel with each development stage of the project. This follows the five ways of working for public bodies, and work to achieving the wellbeing goals, outlined in the Well-Being of Future Generations (Wales) Act 2015.

It is not expected that infliximab will have significant potential negative impact on people based on the protected characteristics of the Equality Act 2010.

Additional factors

Infliximab is not licensed to treat this indication and its use is therefore ‘off label’. Providers should consult the relevant guidance on prescribing unlicensed medicines before any off-label medicines are prescribed.

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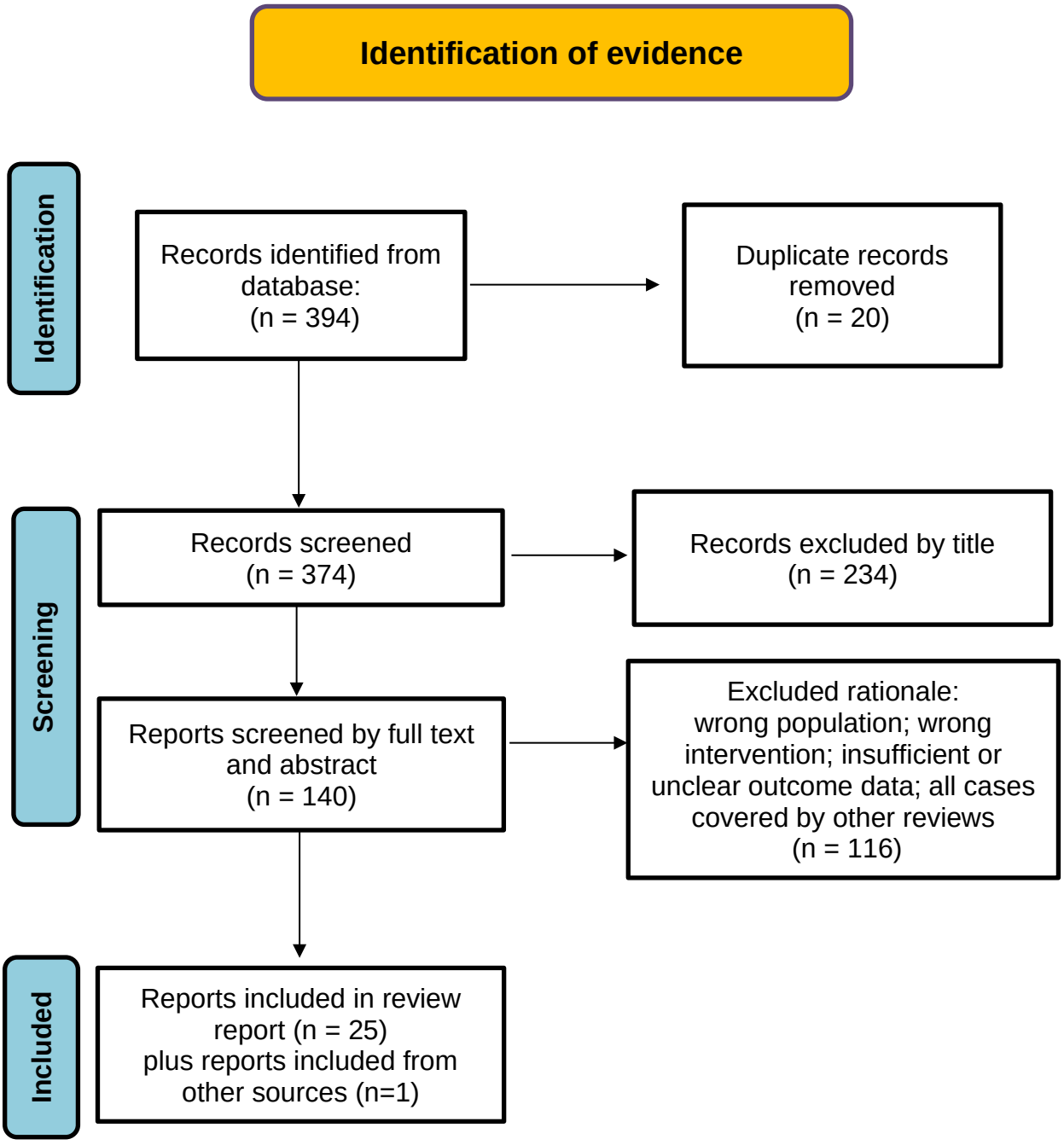
Appendix 1. PRISMA flow diagram – clinical evidence



Appendix 2

Table 2. Case reports and case series of steroid-refractory ICI-induced pneumonitis treated with infliximab

Author (Year)	Study design	Cancer type; (ICI)	Number of patients	Grade of pneumonitis	Steroid refractory	Prior additional treatment	Infliximab dose and number of infusions	Response to infliximab treatment
Case reports and single cases from case series								
Vera et al. (2025)[19]	Case report	Hepatocellular carcinoma; (atezolizumab)	1	4	Yes	IVIG (1 g/kg) for 3 days	Dose: 5 mg/kg No. infusions: 2	No response
Bischin et al. (2025)[14]	Case report	Urothelial carcinoma (pembrolizumab)	1	4	Yes	NR	Dose 1: 5 mg/kg Dose 2: 10 mg/kg No. infusions: 2	Complete response
Adams et al. (2025)[20]	Case series	Not specified	1	NR	Yes	NR	NR	Complete response
Varathalajaru et al. (2025)[12]	Case report	Breast cancer and mesothelioma (nivolumab and ipilimumab)	1	NR	Yes	NR	NR	Partial response
Torres et al. (2024)[18]	Case report	Bladder cancer (nivolumab)	1	NR	Yes	NR	Dose: 5 mg/kg No. infusions: 1 + MMF	Improved with no adverse events
Sharif et al. (2024)[24]	Case report	NSCLC (durvalumab)	1	4	Yes	NR	Dose: NR No. infusions: 2	Gradual improvement

Author (Year)	Study design	Cancer type; (ICI)	Number of patients	Grade of pneumonitis	Steroid refractory	Prior additional treatment	Infliximab dose and number of infusions	Response to infliximab treatment
Case reports and single cases from case series								
Pan et al. (2023)[21]	Case report	NSCLC (camrelizumab)	1	4	Yes	NR	Dose: 500 mg No. infusions: 1	Improved, continued ICI treatment with stable disease
Gökmen et al. (2023)[22]	Case series	Not specified	1	NR	Yes	NR	NR	Improvement
Buntak et al. (2023)[15]	Case report	Oesophageal cancer (nivolumab)	1	NR	Yes	tocilizumab (8 mg/kg)	Dose: 5 mg/kg No. infusions: 1 + IVIG (0.4 g/kg)	Transient improvement
Allen et al. (2023)[25]	Case series	NSCLC ICI not specified	1	4	Yes	NR	Dose: NR No. infusions: NR + cyclophosphamide	No response
Segui et al. (2022)[28]	Case series	Bladder cancer (atezolizumab)	1	NR	Yes	NR	NR	No response
Kunimasa et al. (2022)[11]	Case report	NSCLC (nivolumab and ipilimumab)	1	4	Yes	tocilizumab (8 mg/kg)	Dose: 5 mg/kg No. infusions: 1	Clinical improvement
Shah et al. (2022)[17]	Case report	Hepatocellular carcinoma (atezolizumab)	1	NR	Yes	NR	Dose: 5 mg/kg No. infusions: 1	Clinical improvement
Arana-Riberio et al. (2021)[13]	Case report	NSCLC (pembrolizumab)	1	NR	Yes	NR	Dose: 5 mg/kg No. infusions: 1	No response

Author (Year)	Study design	Cancer type; (ICI)	Number of patients	Grade of pneumonitis	Steroid refractory	Prior additional treatment	Infliximab dose and number of infusions	Response to infliximab treatment
Case reports and single cases from case series								
Nagasunder et al. (2020)[26]	Case report	Melanoma (pembrolizumab)	1	3	Yes	NR	NR	No response
Burdett et al. (2020)[27]	Case series	Not specified	1	NR	Yes	NR	NR	No response
Carrión Madroñal et al. (2019)[16]	Case report	NSCLC (pembrolizumab)	1	4	Yes	NR	Dose: 5 mg/kg No. infusions: 1	No response
Alzghoul et al. (2019)[23]	Case report	NSCLC (durvalumab)	1	4	Yes	NR	Dose: 500 mg No. infusions: 1	Clinical improvement
Case series								
Sun et al. (2025)[29]	Case series	Not specified	4	NR	Yes	NR	NR	No response
Tan et al. (2023)[30]	Case series	Not specified	3	NR	Yes	NR	NR	2 complete response 1 no response
Frost et al. (2023)[31]	Case series	Lung cancer ICI not specified	6	≥ 3	Yes	NR	NR	No response
Sheshadri et al. (2022)[32]	Case series	AML ICI not specified	2	NR	Yes	NR	NR	No response

AML: acute myeloid leukaemia; BD: twice daily; ICI: immune checkpoint inhibitor, IVIG: intravenous immunoglobulin, MMF: mycophenolate mofetil, No.: number; NR: not reported, NSCLC: non-small cell lung cancer