One Wales Medicine Assessment Group summary of decision rationale

Medicine: **infliximab**
Indication: **treatment of grade 3–4 steroid-refractory pneumonitis induced by immune checkpoint inhibitor (ICI) therapy (OW34)**
Meeting date: **6 December 2025**

Criteria	OWMAG opinion
Clinical effectiveness and safety	OWMAG note that there is limited published clinical evidence available for infliximab for the treatment of grade 3–4 steroid-refractory pneumonitis induced by immune checkpoint inhibitor (ICI) therapy and that no randomised controlled trials or comparative studies were identified. Evidence comes from two systematic reviews, four retrospective case series of 15 patients in total and 18 case reports. OWMAG acknowledge the paucity of data to inform comparisons between different second-line immunosuppressive therapy options for this indication. Taking the published evidence as a whole, OWMAG note that between 30-40% of all the patients reported in these studies showed a clinical response to infliximab. OWMAG note the limitations of the evidence and acknowledge that case reports are generally the lowest grade of evidence as they may be subject to selection bias, are difficult to compare, involve small patient numbers, differ in the amount of clinical information given and the outcomes reported, and so may not be generalisable to patients with this condition in Wales. They note that many patients were treated with multiple immunosuppressive agents in addition to steroids making the relative benefit of infliximab difficult to ascertain. OWMAG acknowledge that published clinical guidelines such as those from the European Society for Medical Oncology (ESMO), the American Society of Clinical Oncology (ASCO) and the US National Comprehensive Cancer Network (NCCN), which mainly considered the same published clinical evidence, broadly agree in recommended second-line options and all include infliximab; none of these options are licensed for this indication in the UK. OWMAG note that all guideline recommendations on treatment options are based on low-quality evidence, mainly derived from clinical expert opinion and that clinical opinion can also be informed by preference and experience of using specific treatments. OWMAG note the evidence provided by clinical experts, both in the evidence summary report (ESR) and at the meeting, who report that patients who do not respond to intravenous corticosteroid treatment within 48-72 hours require prompt and effective treatment with an additional immunosuppressant to prevent further deterioration. The current treatment options used in NHS Wales is

	mycophenolate mofetil (MMF) although infliximab or tocilizumab may be used on an individual patient basis. However, MMF takes a couple of weeks to have a clinical effect whereas infliximab is usually fast-acting after one dose. Clinicians in Wales report they have significant experience and familiarity with using infliximab for other ICI-induced toxicities and have had experience of using it for pneumonitis with good clinical responses noted. They also confirmed that response rates from their own clinical practice, and those shared by colleagues from elsewhere in the UK, are much higher than those reported in the published literature. OWMAG note that currently clinicians have to request infliximab on an individual patient basis through local processes which takes time and clinical resource; this can cause delay in initiating treatment and can be detrimental to patient outcomes as patients with this condition can deteriorate rapidly and prompt appropriate treatment is essential. Routine all-Wales access to infliximab will help standardise the treatment pathway in Wales, ensure equity and avoid delay in treatment which may lead to better patient outcomes. OWMAG note that all-Wales guidelines are currently in development by the National Immunotherapy Toxicity Sub-Group on the management of ICI-induced toxicities including pneumonitis. OWMAG note that the use of infliximab (in addition to corticosteroids) is associated with an increased risk of infection and deaths due to infectious complications. OWMAG acknowledge that the NHS Wales National Immunotherapy Toxicity Sub-Group advises that infliximab for the treatment of ICI-induced pneumonitis will only be offered to patients who are not at significant risk of autoimmune infections. For older patients who may be more immunosuppressed, tocilizumab would be used in preference to infliximab as it is less immunosuppressive than infliximab. OWMAG consider that the current published evidence for the use of infliximab to treat grade 3-4 pneumonitis is of very low quality, however, it acknowledges that the published evidence is not reflective of the response rates clinicians are reporting in practice. The experts in attendance state that they are in regular dialogue with other UK clinicians treating patients with this toxicity who all report better outcomes with infliximab than those reported in the literature and that clinical practice is quickly evolving in this area and based on real world experience which the published evidence base is not keeping up with. Taking into account the limited published evidence available, the real world experience reported by clinicians and the safety considerations highlighted, OWMAG consider infliximab

	demonstrates some clinical effectiveness as a treatment option for this indication and that the benefits of its use outweigh the risks.
Cost-effectiveness	OWMAG note that no comparative cost-effectiveness evidence was identified for this use of infliximab, and in the absence of any comparative studies of infliximab for this indication, no cost effectiveness analyses were undertaken by AWTTC. OWMAG consider that the likely costs associated with using infliximab for this indication would be reasonable in considering the potential benefit gained from this intervention.
Budget impact	OWMAG consider the clinical estimate of patient numbers reported to be reasonable. However, OWMAG note that use of ICI-treatments are likely to increase in future years, treatment-related toxicities including pneumonitis are also likely to increase. Therefore, patient numbers are expected to rise with an accompanying increase in budget impact. OWMAG note additional screening, monitoring and adverse event costs are excluded from the budget impact calculations both for infliximab and for comparator treatments. In particular, clinicians state that from their experience, patients with grade 3-4 pneumonitis unresponsive to steroids will deteriorate and they will require intensive in-hospital treatment for several days or weeks. Infliximab treatment may cause a rapid improvement in pneumonitis symptoms enabling prompt hospital discharge. OWMAG note that the degree of displacement of the comparator treatment MMF is difficult to estimate and that clinicians indicate that some patients would receive MMF and infliximab simultaneously. However, the acquisition cost of MMF is low and has very little effect on the overall budget impact. Also, from the clinical opinion provided, OWMAG note that it's likely not all patients will receive three doses of infliximab; therefore, the budget impact may be overestimated. OWMAG also acknowledge that 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. OWMAG consider that the base case provided in the report is a reasonable estimate of the associated cost to NHS Wales.
Resource use	OWMAG note that infliximab is given by intravenous infusion in a healthcare setting whereas some comparator treatments are taken orally. However, due to the severity of

	the condition, patients with grade 3–4 ICI-induced pneumonitis are likely to initially be hospital in-patients and so the addition of the first dose of infliximab to the treatment pathway is likely to have a low additional impact. It is expected that subsequent doses can be administered as an outpatient. As previously mentioned, the use of infliximab may shorten hospital stay in comparison to patients receiving MMF alone.
Other factors	OWMAG acknowledges that pneumonitis is a rare but serious complication of ICI therapy. Pneumonitis is potentially fatal and early assessment and intervention are key as patients with this condition can deteriorate rapidly. Whilst patients will generally accept significant toxicities in order to live longer, effective and early interventions are needed to improve patient quality of life and outcomes. OWMAG also acknowledges the testimony of the patient organisation representative who highlighted the ease of access to infliximab for this indication for patients treated in England. She also highlighted that pneumonitis, which causes patients to struggle for breath, is particularly unpleasant and frightening and that prolonged intensive in-hospital treatment can lead to psychological distress. Both the patient organisation representative and the clinical experts present also mentioned that prompt treatment with infliximab may avoid some long-term or lifelong side effects from the prolonged use of high-dose steroids and from the pneumonitis itself. OWMAG notes that, due to the mechanism of action of ICIs, patients who develop a severe toxicity are much more likely to exhibit a prolonged response to ICI treatment with many patients living ten or more years. This is in contrast to a predicted overall survival of several months before ICI treatments became available. However, clinicians highlight that the effective management of the toxicities that ICI treatments may induce is crucial in being able to realise the benefits these treatments offer. OWMAG recognises that a standardised NHS Wales treatment pathway for pneumonitis unresponsive to steroids will ensure that appropriate and swift second-line immunosuppression treatment can be given which will help avoid unnecessary long-term complications or death. Making infliximab routinely available for this group of patients will avoid potential delays in getting access, freeing up clinician time and enabling prompt and equitable access for patients across Wales. There are no licensed alternative treatment options routinely available.

Final recommendation	OWMAG recommend the use of infliximab for the treatment of grade 3–4 steroid-refractory pneumonitis induced by immune checkpoint inhibitor (ICI) therapy. This recommendation is subject to the development of appropriate start/stop criteria.
Summary of rationale	Although the published evidence to support the use of infliximab for the treatment of ICI induced grade 3-4 pneumonitis where symptoms have not responded to first-line immunosuppression with corticosteroids is limited and of very low quality, OWMAG considers that the real world experience of clinicians using infliximab for this indication, offers additional supportive evidence of its clinical effectiveness. There are no licensed alternative treatment options and international guidelines recommend the use of infliximab for this indication. Allowing routine access to infliximab will help standardise the treatment pathway in Wales and may enable earlier initiation of treatment resulting in improved patient outcomes. Due to the known increased risk of infections associated with infliximab, clinicians in Wales propose using it only in patients who are not at significant risk of autoimmune infections. The review after 12 months will provide the number of patients who have received this treatment in Wales and more evidence on whether this is an effective treatment for this patient population.