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

One Wales Medicines Assessment Group (OWMAG)
Minutes of the Teams meeting held Monday, 8 December 2025

Members in attendance
Andrew Champion, Program Director, AWTTC, Interim OWMAG Chair
Tim Banner, Clinical Director Pharmacy & Medicines Management, representative Cardiff and Vale
Maggie Clark, Head of Access & Adoption Policy (Devolved Nations), ABPI
Stuart Wyn Evans, Clinical Effectiveness Pharmacist, representative Swansea Bay
Laurence Gray, Clinical Pharmacologist
Will Hardy, Research Fellow, Bangor University, Health Economist
Brian Hawkins, Chief Pharmacist Medicines Governance, representative Cwm Taf Morgannwg
William King, Consultant in Public Health, representative Powys
Malcolm Latham, Lay representative
Anghard Lawson, Advanced Pharmacist, NHS Wales Joint Commissioning Committee
Susan Myles, Director, Health Technology Wales
Craig Roberts, Assistant Director of Allied Health Professions & Health Science, representative Aneurin Bevan
Michael Thomas, Consultant in Public Health, representative Hywel Dda

AWTTC
Eleri Burd, Advanced Pharmacist
Clare Elliott, Senior Scientist
Laura Phillips, Admin Manager
Jessica Waddington, Medical Writer
Gail Woodland, Senior Pharmacist

Clinical experts
Dr Ricky Dylan Frazer
Dr Carey McDonald-Smith

Patient Organisation representative
Jackie Hodgetts

List of abbreviations:

ABPI	Association of the British Pharmaceutical Industry
AWMSG	All Wales Medicines Strategy Group
AWTTC	All Wales Therapeutics and Toxicology Centre
ESR	Evidence status report
ICI	immune checkpoint inhibitor
IPFR	Individual Patient Funding Request
IVIG	Intravenous immunoglobulin
MMF	Mycophenolate mofetil
NICE	National Institute for Health and Care Excellence
OWMAG	One Wales Medicines Assessment Group

RCT Randomized controlled trial

Welcome and introduction
The Chair opened the meeting and welcomed members.

Apologies
- Chris Commins, Assistant Finance Director, Aneurin Bevan
- Kathryn Howard, Head of Pharmacy, Royal Glamorgan Hospital, representative Cwm Taf Morgannwg
- Hazel Jones, lay representative
- Leo Pinto, Consultant in Public Health, representative Aneurin Bevan

Welcome
Dr Andrew Champion welcomed the Group and the meeting observers. He gave an update on actions since the previous OWMAG meeting: AWMSG endorsed the recommendation by OWMAG to recommend the use of venetoclax with azacitidine for the treatment of relapsed/refractory acute myeloid leukaemia in adults following at least one line of intensive chemotherapy before or following allogenic haematopoietic stem cell transplant (HSCT) where it is not appropriate to offer intensive chemotherapy. This has now been ratified by Welsh Government. The OWMAG external review recommendation for rituximab for the treatment of myasthenia gravis in adults was also endorsed by AWMSG and ratified by Welsh government. The current advice is to be retained with no changes and will be reviewed again in 12 months.

Declarations of interests/confidentiality
The Chair reminded members that all OWMAG proceedings are confidential and should not be disclosed outside of the meeting. Members were reminded that declarations of interest and confidentiality statements are signed by each member on an annual basis. The Chair invited any declarations of interest relating to the medicine being assessed today; there were none.

Assessment
Infliximab for the treatment of Immune Checkpoint Inhibitor (ICI) induced grade 3-4 pneumonitis that has not responded to first line immunosuppression with corticosteroids

The Chair introduced the medicine to be assessed: infliximab, and welcomed Dr Carey McDonald-Smith, Associate Specialist in Medical Oncology and Immunotherapy lead for the North Wales Cancer Treatment Centre and Dr Ricky Dylan Frazer, Consultant Medical Oncologist and Clinical Lead for the South East Wales Immunotherapy Toxicity Service, to the meeting. The Chair described the role of the clinical expert as an invited observer of the OWMAG meeting to answer questions and input into discussions to enable members to gain a better understanding of the clinical context. The Chair highlighted that clinical experts were nominated by their specialist group or network and should not express their personal opinion or promote the use of a medicine. The Chair invited any declarations of interest from Dr McDonald-Smith and Dr Frazer; there were none.

The Chair invited Clare Elliott to present the assessment of infliximab. Clare Elliott presented the key aspects of the clinical effectiveness section of the evidence status report (ESR). Clare briefly explained current treatment options given in some international guidelines for steroid-refractory ICI-induced pneumonitis. She explained that infliximab is recommended in all as a second-line immunosuppressant option but there is a paucity of data to inform comparisons between all the different options included and the recommendations in all guidelines are based on low-quality evidence mainly derived from clinical expert opinion, preference and experience. Clare confirmed that there are no RCTs published for infliximab for this treatment and evidence comes from systematic reviews, retrospective case series and case reports with some limited real-world outcomes from NHS Wales. Clare highlighted that published response rates for infliximab were between 30-40% but that a high fatality rate from severe pneumonitis is observed regardless of the second-line immunosuppressive agent used. She also gave details of the safety profile of infliximab and that, because of the well-known risk of infection, older patients more at risk of autoimmune infections would receive an alternative, less immunosuppressant agent in preference to infliximab. In conclusion, she summarised that the published evidence is low quality and inconclusive and that comparisons between agents is difficult.

The Chair invited the clinical experts, Dr Carey McDonald-Smith and Dr Ricky Frazer, to tell the Group about their experiences in treating patients with steroid-refractory ICI-induced pneumonitis, what medicines they currently use for treatment and how infliximab would add to the armoury of treatment options.

Dr Frazer provided some clinical context with regard to ICI therapy and how their use is widespread and has been transformative in the treatment of many cancers with people who respond to treatment likely to survive long term. He highlighted that ICIs are associated with significant toxicities as the immune system activation targeting the cancer also causes immune responses in other organs; severe toxicity often correlates with better cancer outcomes as long as the patient survives the toxicity. He confirmed that severe pneumonitis has a high mortality rate and standard treatment is with steroids. Dr Frazer stated that from his clinical experience about 20% of patients with severe pneumonitis do not respond to steroids and require a second-line immunosuppressant agent; these patients also deteriorate rapidly and require a very prompt and quick-acting treatment. Dr Frazer gave an overview of the classes of second line treatment options, these being anti-cytokine alpha TNFs (e.g infliximab), T-cell directed therapies (e.g MMF) and B-cell directed therapies (e.g IVIG) and that anti-cytokine therapies are used first due to their speed of response, usually within 24 hours, in comparison to the other classes of therapy which can take several days. Dr Frazer stated that he is involved in a UK-wide peer-to-peer clinical group for the management of patients with complex ICI-induced toxicities and that infliximab is the most commonly used second line agent for the treatment of steroid-resistant pneumonitis. From real world experience reported in this national group, the data suggests that infliximab treatment is successful in about 60% of patients with severe steroid-resistant pneumonitis. He highlighted the importance of having optimal pathways to manage these predictable toxicities and standard mechanisms to access

infliximab in Wales to avoid unnecessary delay in initiating treatment which is likely to have a detrimental effect on the outcome of the patient. Dr Frazer mentioned that a number of patients who would have benefitted from infliximab treatment in South East Wales were unable to receive it due to delays in access.

Dr McDonald-Smith agreed with the points raised by Dr Frazer and also described struggles in accessing infliximab for patients identified as steroid unresponsive and requiring additional therapies from North Wales and how this makes managing such patients problematic. Dr McDonald-Smith highlighted the importance of having early and easier access to infliximab to improve outcomes for patients throughout the whole of Wales.

A member of the Group asked about the treatment pathway and whether it was patient-specific or linear in treatment options. Both clinicians agreed that it was patient-specific after non-response to first-line steroid treatment and dependant on the severity of the pneumonitis and the rate of deterioration. Infliximab would be the preferred treatment choice for patients with severe pneumonitis who are deteriorating rapidly due to its quick onset of action. In response to another query about how this indication is managed elsewhere in the UK, Dr Frazer confirmed that there is at least one case of pneumonitis being managed with infliximab across the UK each week and that there is easy access to it (and tocilizumab) in England for refractory pneumonitis.

A member of the Group asked what the outcomes are generally for patients with severe steroid-resistant pneumonitis not treated with infliximab. Both clinicians agreed that such patients would require treatment on HDU or ITU for several days as they would require intubation or respiratory support, and those that survived would require treatment on general wards for another couple of weeks. A number may develop lung disease from the pneumonitis requiring long-term medication and which may impact quality of life and normal daily activities such as working, and preclude further cancer treatments. These patients will also require steroid treatment for longer with the risk of steroid-induced toxicity which can impact quality of life and increase the risk of sustained infections.

A query was raised by a Group member on the difference in clinical response rates reported in the published literature and those reported by clinicians from real world experience. Both clinicians replied that the use of immunotherapy in general and the treatment of arising toxicities is a fast-moving area of clinical practice, advancements in the management of toxicities are being shared between clinicians via clinical networks and forums and there is a delay in publishing the emerging real-world evidence in peer-reviewed journals. Therefore, the published evidence base is some way behind accepted best clinical practice in the UK. Both Clare Elliott and the Chair emphasised to members that clinical experience is a form of evidence and should be taken into account in their decision-making. Gail Woodland, AWTTC lead for the One Wales assessment process, also reminded the Group that all recommendations made by OWMAG are interim and regularly reviewed to see if there is any new evidence that may call it into question; the first review happens 12 months after

publication of the recommendation. This includes searching the literature for any new relevant published evidence, and if a positive recommendation, the collection of patient numbers and outcomes from use of the treatment in NHS Wales. These data can be used to inform whether the presumed benefits and value of the treatment are realised in practice. Each recommendation is also accompanied by a published decision rationale which sets out why OWMAG reached the decision it did, and clinical starting and stopping criteria which specifically state, amongst other things, the eligibility criteria to start a patient on treatment, criteria for stopping treatment and the type of outcome data that should be collected by clinicians.

The Chair concluded questions about the clinical effectiveness and asked Clare Elliott to present the cost-effectiveness evidence and budget impact. Clare Elliott explained that there were no published cost-effectiveness studies. She presented the budget impact, which estimated costs for 12 patients per year in Wales. Clare explained that the degree of displacement of the comparator treatment MMF is difficult to estimate, and some patients may receive both infliximab and MMF. However, due to the low acquisition costs of MMF, the impact of MMF on the overall budget impact is negligible. From the experience of clinicians, not all patients will receive three doses of infliximab, therefore the budget impact may be overestimated. Due to the lack of comparative data between treatments, any additional benefit from infliximab cannot be quantified and taken into account in budget impact calculations.

One member asked about the costs of treating serious infections, such as sepsis arising from immunosuppressant treatment. Dr McDonald-Smith said that all patients on immunosuppressants or long-term steroids would be on prophylactic antibiotics and the costs would not be specific to infliximab. Dr Frazer confirmed that in his experience, patients who died from sepsis or other opportunistic infections were those that had been on steroids for a prolonged time and both clinicians agreed that reducing steroid burden by getting patients on infliximab earlier would reduce risk of infection.

Clare Elliott presented the wider health and social aspects highlighting that 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. Pneumonitis is a serious and potentially fatal toxicity and early assessment and intervention is key. A standardised NHS Wales treatment pathway which includes routine access to infliximab will ensure that appropriate and swift second-line immunosuppression treatment can be given. She also said that the equality and health impact assessment did not find any potential negative or an unequal impact on people based on their protected characteristics and would expect a potential positive impact on people with ICI-induced pneumonitis and their families and carers.

The Chair invited Jackie Hodgetts, representative of Melanoma Focus and also an oncology nurse specialist at the Christie Hospital in Manchester, to give the views of patients affected with this toxicity. Jackie stated that pneumonitis tends to have a fairly rapid onset and patients can become very ill very quickly and often have to be treated in intensive or critical care. She 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. Jackie 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 which can have a significant impact on quality of life and which may require frequent admissions to hospital for treatment. From her clinical experience, Jackie also reiterated the complexity of such cases and the importance of clinical experience and expertise built up over years for the effective management of this toxicity, and which published evidence doesn't always reflect.

The Group's lay member was then invited to provide comment on the patient and public perspective. The lay member highlighted the inequity of quick access to infliximab in Wales compared to England and that having unnecessary bureaucracy to access is difficult to justify for a treatment that should be given without delay for maximum benefit. There seems to be a consensus across the UK about using this treatment and it may reduce steroid-dependency which is of benefit to patients. The lay member stated that as infliximab is not an expensive medicine, the public perception would be that is an acceptable level of cost for the benefit it offers. The lay member said he thought there were no good reasons for not making infliximab routinely available for this group of patients.

The Chair thanked Dr McDonald-Smith, Dr Frazer and Jackie Hodgetts who then left the meeting. The Chair summarised the main points of the assessment and the Group took the opportunity to further discuss the points previously raised.

The Chair asked the Group if there were any outstanding issues that required discussion before the vote was opened for the infliximab assessment. The OWMAG recommendation to go to the All Wales Medicines Strategy Group (AWMSG) for endorsement was agreed.

Date of advice: Monday 8 December 2025

Using the agreed starting and stopping criteria infliximab can be made available within NHS Wales for the treatment of grade 3–4 steroid refractory pneumonitis induced by immune checkpoint inhibitor (ICI) therapy.

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.

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 12 months or earlier if new evidence becomes available.

The Group acknowledged that the review of the recommendation after 12 months will provide more evidence on the effectiveness of infliximab and its associated costs for this intervention in NHS Wales. Drafts of the recommendation for endorsement by AWMSG and the decision rationale will be circulated to members after the meeting for comment before final sign-off.

The Chair thanked the Group and closed the meeting.