

Equality and Health Impact Assessment

Infliximab for the treatment of grade 3–4 steroid-refractory myocarditis induced by immune checkpoint inhibitor (ICI) therapy

AWTTC will fill in an Equality and Health Impact Assessment in parallel with each development stage of our projects. This will help us to follow 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.

Date: 16/06/2025

1.	AWTTC contact details	Tel: 02921 826900 Email: awttc@wales.nhs.uk
2.	State the objectives of the project.	To assess the use of infliximab to treat grade 3–4 steroid-refractory myocarditis induced by immune checkpoint inhibitor (ICI) therapy. AWTTC will conduct a literature search for evidence and prepare an evidence status report (ESR) for an assessment under the One Wales Medicines process. The ESR will summarise: current use of infliximab in NHS Wales; evidence of clinical effectiveness and cost effectiveness; safety considerations; budget impact; and equity of access across Wales and the rest of the UK. AWTTC will request the views of relevant patient organisations, and send the ESR to the company (marketing authorisation holder) and to clinicians in Wales for comment. Clinicians, company representatives and patient organisation representatives will be invited to attend the meeting of the One Wales Medicines Assessment Group (OWMAG) to consider the ESR. The OWMAG constitution is available online .
3.	Evidence and background information considered. For example: • population data	Cardiovascular complications, including myocarditis, are rare but potentially life-threatening immune-related adverse events caused by ICI treatment. Mortality is high, with death frequently because of refractory arrhythmia or cardiogenic shock. ICI-induced myocarditis usually presents in the first four



- staff and service users' data, as applicable
- needs assessment
- engagement and involvement findings
- research
- good practice guidelines
- participant knowledge
- list of stakeholders and how stakeholders have engaged in the development stages
- comments from those involved in the designing and development stages

[Population pyramids](#) are available from Public Health Wales Observatory.

cycles of ICI treatment, although a quarter of cases present after four cycles. Severe myocarditis occurs in <1% of patients receiving ICI therapy.

According to the European Society for Medical Oncology (ESMO) [guideline for managing toxicities from immunotherapy](#), ICIs should be discontinued in moderate (grade 2) and severe (grades 3 and 4) cases of myocarditis, and immediate immunosuppressive treatment started; this is vital to avoid irreversible immune-mediated damage to the heart. First-line treatment is with high-dose intravenous corticosteroids; nearly 50% of cases of ICI-induced myocarditis will improve in response to steroid treatment (Tan et al). For patients who do not respond (defined by ESMO as troponin rising or <50% reduction from peak), the ESMO guideline recommends additional second-line immunosuppressive therapy, such as: tocilizumab (8 mg/kg) or mycophenolate mofetil (MMF); third-line treatment options are: alemtuzumab, abatacept or anti-thymocyte globulin (ATG).

For patients without an immediate response to high-dose steroids, an updated [guideline](#) of the American Society of Clinical Oncology (ASCO) considers using methylprednisolone 1 g daily and the addition of either mycophenolate, infliximab or ATG, and to consider abatacept or alemtuzumab as additional immunosuppression in life-threatening cases. A qualifying statement adds that: treatment recommendations are based on anecdotal evidence and the life-threatening nature of cardiovascular complications. Holding checkpoint inhibitor therapy is recommended for all grades of complications. The appropriateness of rechallenging remains unknown. It notes that infliximab has been associated with heart failure and is contraindicated at high doses (i.e., 5 mg/kg) in patients with moderate-severe heart failure.

The Society for Immunotherapy of Cancer (SITC) [clinical practice guideline on ICI-related adverse events](#) recommends that: if signs or symptoms do not respond to corticosteroid therapy within 24 hours, additional therapies such as ATG, mycophenolate mofetil, abatacept, or alemtuzumab should be



considered as additional treatment. Caution is advised against the use of infliximab for steroid-refractory myocarditis.

The National Comprehensive Cancer Network (USA) [guideline on the management of immunotherapy-related toxicities](#) states that immunotherapy should be permanently discontinued for any grade 3 or 4 cardiovascular immune-related adverse events (irAEs). If no improvement is noted within 24 hours of starting high-dose corticosteroid treatment, the addition of other potent immunosuppressive agents should be considered, such as antithymocyte globulin (ATG) infliximab, intravenous immunoglobulin (IVIG) or mycophenolate. Infliximab has been used in case studies to treat cardiotoxicities, but it is important to note that it is contraindicated for patients who have heart failure.

Wales' National Immunotherapy Toxicity Sub-Group submitted the request to consider off-label infliximab for the treatment of ICI-induced myocarditis that has not responded to first line immunosuppression with corticosteroids. The Sub-Group estimates that approximately 42 patients with steroid-resistant grade 3–4 ICI-induced myocarditis across Wales would be eligible for treatment with infliximab each year. However, tocilizumab would be used for patients with an ejection fraction of less than 40%. Clinicians estimate that one in 5 patients would be treated with tocilizumab, meaning that approximately 34 patients per year would receive infliximab.

Infliximab is an anti-tumour necrosis factor-alpha (anti-TNF) antibody licensed to treat a range of chronic immune-mediated inflammatory conditions including Crohn's disease, rheumatoid arthritis, psoriasis and ulcerative colitis. It is not licensed to treat ICI-induced myocarditis – its use in this indication is 'off-label'.

Several infliximab biosimilars are available in NHS Wales. The dose of infliximab is 5 mg/kg administered by IV infusion. A second dose may be repeated 14 days later, with a maximum of three infusions to be given (weeks



		<p>0, 2 and 6). This is the same dosing regimen as for the treatment of ICI-induced enterocolitis (OW21).</p> <p>Clinicians from Velindre Cancer Centre indicate that oral off-label mycophenolate mofetil (MMF) or oral off-label tacrolimus are most commonly used in Wales as second-line treatment for steroid-resistant ICI-induced myocarditis, although infliximab and tocilizumab are also accessed ad hoc. The lack of a treatment pathway means that there isn't an established standard practice in NHS Wales for second-line treatment. 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. Tacrolimus is usually initiated at a dose of 3 mg twice daily and adjusted according to trough levels. High-dose intravenous steroids are given concomitantly for one to two weeks before switching to oral formulations. Treatment with MMF or tacrolimus is continued until the patient has been weaned off steroids and is stable; this is usually between 8–12 weeks after initiation of treatment.</p> <p>The National Immunotherapy Toxicity Sub-Group is currently developing an all-Wales consensus guideline on the management of ICI-induced myocarditis.</p>
<p>4.</p>	<p>Who will this project affect?</p>	<p>People in Wales who develop grade 3 or 4 myocarditis during ICI therapy for cancer, and their families and carers.</p>



5. EQIA - How will the project impact on people?

Questions in this section relate to the impact on people based on the 'protected characteristics' of the Equality Act 2010, and other factors.

How will the project impact on, or affect:	Potential positive and/or negative impacts	Recommendations for improvement/ mitigation	Actions taken (and who by).
<p>5.1 Age For most purposes, the main categories are people aged:</p> <ul style="list-style-type: none">• under 18 years;• between 18 and 65 years;• over 65 years.	<p>We do not expect a potential negative, or unequal, impact on people based on their age.</p> <p>[Note: For prescription medicines we expect the prescriber to have prescribed or advised their use within the terms of their UK marketing authorisations. Healthcare professionals should take note of the contraindications, warnings, safety recommendations and any monitoring needs for the medicine. These are explained in the Summary of Product Characteristics (SmPC) for the medicine or the British National Formulary.</p>	<p>N/A</p>	<p>N/A</p>



How will the project impact on, or affect:	Potential positive and/or negative impacts	Recommendations for improvement/ mitigation	Actions taken (and who by).
	<p>The use of infliximab for the indication assessed is off-label. Healthcare professionals should follow relevant professional guidance and take full responsibility for the decision when prescribing or advising the use of off-label or unlicensed medicines. This includes considering the contraindications, warnings, monitoring requirements and other safety recommendations for the medicine (MHRA guidance on off-label or unlicensed use of medicines)</p>		
<p>5.2 Persons with a disability as defined in the Equality Act 2010 Those with physical impairments, learning disability, sensory loss or impairment, mental health conditions, long-term medical conditions such as diabetes.</p>	<p>We do not expect a potential negative, or unequal, impact on people with a disability.</p>	<p>All related documents published on the AWTTC website will meet accessibility requirements.</p> <p>Any patient-facing materials will be also be produced as easy</p>	<p>N/A</p>



How will the project impact on, or affect:	Potential positive and/or negative impacts	Recommendations for improvement/ mitigation	Actions taken (and who by).
		read booklets in Welsh and English.	
5.3 People of different genders: Consider men, women, people undergoing gender reassignment. N.B. Gender-reassignment is anyone who proposes to, starts, is going through or who has completed a process to change his or her gender with or without going through any medical procedures. Sometimes referred to as Trans or Transgender.	We do not expect a potential negative, or unequal, impact on people based on their gender, or on people undergoing gender reassignment.	N/A	N/A
5.4 People who are married or who have a civil partner.	We do not expect a potential negative, or unequal, impact on people based on their marital status or being in a civil partnership.	N/A	N/A
5.5 Women who are expecting a baby, who are on a break from work after having a baby, or who are breastfeeding.	We do not expect a potential negative, or unequal, impact on women who are expecting a baby, are breastfeeding, or are	Prescribers should take account of the Summary of Product Characteristics (SmPC) when prescribing any	The SmPC criteria specify which people are excluded from treatment due to the associated risks of treatment.



How will the project impact on, or affect:	Potential positive and/or negative impacts	Recommendations for improvement/ mitigation	Actions taken (and who by).
They are protected for 26 weeks after having a baby whether or not they are on maternity leave.	<p>on a break from work after having a baby.</p> <p>Infliximab should only be used during pregnancy if clearly needed. Please refer to the SmPC.</p> <p>Infliximab could be considered for use during breast-feeding.</p> <p>The SmPC advises that women of childbearing potential should consider the use of adequate contraception to prevent pregnancy and continue its use for at least 6 months after the last infliximab treatment.</p>	medicines for women who are pregnant, or who are breastfeeding.	This will be identified for consideration of any change to the advice at the next review if there is a change to the current advice for pregnant and breastfeeding women.
5.6 People of a different race, nationality, colour, culture or ethnic origin including non-English speakers, gypsies and travellers, migrant workers. The Runnymede Trust	We do not expect a potential negative, or unequal, impact on people of a different race, nationality, colour, culture or ethnic origin.	Note in the project document that people of different race and ethnicities can have varying responses to medicines.	N/A



How will the project impact on, or affect:	Potential positive and/or negative impacts	Recommendations for improvement/ mitigation	Actions taken (and who by).
	People of different race and ethnicities can have varying responses to medicines.		
5.7 People with a religion or belief or with no religion or belief. The term 'religion' includes a religious or philosophical belief. Implications of religious beliefs on selection of medicines (BMJ) In practice: guidance on religion, personal values and beliefs (General Pharmaceutical Council)	We do not expect a potential negative, or unequal, impact on people who have a religion or belief, or people with no religion of belief. Some medicines are made from certain animal products and people might not want to take them because of religion or belief.	N/A	N/A
5.8 People who are attracted to other people of: <ul style="list-style-type: none">• the opposite sex (heterosexual);• the same sex (lesbian or gay);• both sexes (bisexual). Stonewall	We do not expect a potential negative, or unequal, impact on people based on who they are attracted to.	N/A	N/A
5.9 People who communicate using the Welsh language in terms of correspondence, information leaflets, or service plans and design.	We do not expect a potential negative, or unequal, impact on people who communicate using the Welsh language.	Any patient-facing materials will be produced in Welsh and English, in line with the Welsh	N/A



How will the project impact on, or affect:	Potential positive and/or negative impacts	Recommendations for improvement/ mitigation	Actions taken (and who by).
	Any patient-facing materials will be produced in Welsh and English, in line with the Welsh language standards, including easy read booklets.	language standards, including easy read booklets.	
5.10 People according to their income related group.	We do not expect a potential negative, or unequal, impact on people based on their income-related group. In Wales, all prescription medicines are free-of-charge for patients; positive recommendations through this project will not affect people depending on their income-related group.	N/A	N/A
5.11 People according to where they live.	We do not expect a potential negative, or unequal, impact on people based on where they live.	N/A	N/A
5.12 Consider others who face health inequalities, such as:	We do not expect a potential negative, or unequal, impact on	N/A	N/A

How will the project impact on, or affect:	Potential positive and/or negative impacts	Recommendations for improvement/ mitigation	Actions taken (and who by).
<ul style="list-style-type: none"> • Looked after and accommodated children and young people • Carers: paid/unpaid, family members • People who are homeless or those who experience homelessness: people on the street; those staying temporarily with friends/family; those in hostels/B&Bs • People involved in the criminal justice system: offenders in prison or on probation, ex-offenders • People with addictions and substance misuse problems • People who have poor literacy • People living in remote, rural and island locations 	people who face health inequalities.		
5.13 Consider any other groups and risk factors relevant to this project.	N/A	N/A	N/A

6. HIA - How will the project impact on the health and wellbeing of people in Wales and help address inequalities in health?

Questions in this section relate to the impact on the overall health of individual people, and the impact on the population in Wales.



How will the project impact on, or affect:	Potential positive and/or negative impacts and any particular groups affected	Recommendations for improvement/ mitigation	Actions taken (and who by) <i>Refer to where the mitigation is included in the document, as appropriate.</i>
6.1 People being able to access the service offered.	We do not expect a potential negative, or unequal, impact on people's ability to access the service offered.	N/A	N/A
6.2 People being able to improve or maintain healthy lifestyles.	We do not expect a potential negative, or unequal, impact on people's ability to improve or maintain healthy lifestyles.	N/A	N/A
6.3 People in terms of their income and employment status.	We do not expect a potential negative, or unequal, impact on people in terms of their income and employment status.	N/A	N/A
6.4 People in terms of their use of the physical environment.	We do not expect a potential negative, or unequal, impact on people's use of the physical environment.	N/A	N/A
6.5 People in terms of social and community influences on their health.	We do not expect a potential negative, or unequal, impact on people in terms of social and community influences on their health.	N/A	N/A
6.6 People in terms of macro-economic, environmental and sustainability factors.	We do not expect a potential negative, or unequal, impact on people in terms of macroeconomic, environmental and sustainability factors.	N/A	N/A

7. Please fill in section 7.1 after completing the EqHIA, and fill in the action plan.

7.1 Please summarize the potential positive and/or negative impacts of the project.	No potential negative impacts identified.
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Action plan for mitigation or improvement and implementation

	Action	Lead(s)	Timescale	Actions taken (<i>state who by</i>)
7.2 What are the key actions identified as a result of completing the EqHIA?	<ul style="list-style-type: none"> • Consult with clinical experts in Wales, patient organisations, patients and carers in Wales (or the UK) and invite comments through the AWTTC website. • AWTTC to prepare an Evidence Summary Report (ESR) • One Wales Medicines Assessment Group (OWMAG) meet to consider. • AWMSG meet to ratify OWMAG's recommendation. 	AWTTC	Jun-Jul 2025 Jun-Jul 2025 Aug 2025 Sep 2025	
7.3 Is a more comprehensive Equalities Impact Assessment or Health	No			

	Action	Lead(s)	Timescale	Actions taken (<i>state who by</i>)
Impact Assessment needed?				
7.4 What are the next steps?	AWTTC to write an evidence summary report for consideration by the One Wales Medicines Assessment Group (OWMAG).	AWTTC	Jun-Jul 2025	
7.5 Review of project and EqHIA		AWTTC	12 months after publication of recommendation	

AWTTC's EqHIA template is adapted from the Cardiff & Vale University Health Board EHIA template.