Grŵp Strategaeth Meddyginiaethau Cymru Gyfan
All Wales Medicines Strategy Group

One Wales Medicines Assessment Group Recommendation
Azacitidine for the treatment of progressive angioimmunoblastic T-cell lymphoma (OW16)

Date of advice: July 2020
Date of last review: February 2026
AWTTC reference number: OW16

Using the agreed starting and stopping criteria, azacitidine can be made available within NHS Wales for the treatment of progressive angioimmunoblastic T-cell lymphoma.

The risks and benefits of the off-label use of azacitidine 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 recommendation has been endorsed by the All Wales Medicines Strategy Group (AWMSG) and ratified by Welsh Government.

This advice has been reviewed 3 times by OWMAG since its issue in 2020 with no new evidence identified to affect the current recommendation. Therefore, this advice will no longer undergo review by OWMAG unless new evidence becomes available.

Health board responsibility
Health boards will take responsibility for implementing One Wales Medicines Assessment Group decisions.

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One Wales advice assists consistency of access across NHS Wales.

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Starting and stopping criteria for azacitidine for the treatment of progressive angioimmunoblastic T-cell lymphoma

These criteria have been developed with support from Consultant Haematologists in Wales.

Starting criteria:
Second and subsequent line therapy of patients with relapsed/refractory angioimmunoblastic T-cell lymphoma (AITL) that are not fit or suitable for intensification of therapy with a BEAM (carmustine [BCNU], etoposide, cytosine arabinoside [Ara-C] and melphalan) conditioned autograft. Azacitidine should only be considered if the patient is ineligible to enrol in a clinical trial.

Patients who satisfy the eligibility criteria will be prescribed azacitidine following consultation with the patient and/or carer taking into account potential adverse effects, cautions and contraindications. This consultation should be recorded in the patient's notes.

Azacitidine is prescribed at a dose of 75 mg/m^2, injected subcutaneously, daily for 7 days followed by a 21 day rest period. It may be appropriate to administer this treatment as 5 days on, weekend off, 2 days on, to avoid higher administration costs over the weekend.

The Cheson criteria is used to classify AITL response to treatment, the treatment goal is remission[1]. In summary, a complete response (CR) is defined as the disappearance of all evidence of disease, a partial response (PR) is a regression of measurable disease and no new sites. Stable disease (SD) is a failure to attain CR/PR or progressive disease (PD). PD or relapsed disease is an increase by ≥ 50% of measurable signs of the disease from nadir. Overall response rate represents both CR and PR[1].

Prescribers will be expected to provide outcome data on all patients who receive azacitidine treatment under the One Wales Medicines process.

Stopping criteria:
Treatment should be reviewed after three cycles and azacitidine stopped if any of the following criteria are met:

- clinical evidence of disease progression/relapse in accordance with the Cheson response criteria[1].
- toxicity
- patient request

At 12 months treatment should be reviewed to consider whether there is continued clinical benefit for the patient and no evidence of disease progression.

Reference

1. Cheson B, Pfistner B, Juweid M et al. Revised response criteria for malignant lymphoma. *Journal of Clinical Oncology.* 2007;25(5):579-586.

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Third Review of One Wales Decision – January 2026
Azacitidine for the treatment of progressive angioimmunoblastic T-cell lymphoma (OW16)

This report was prepared by the All Wales Therapeutics and Toxicology Centre (AWTTC) in December 2025. It summarises any new evidence available and patient outcome data collected since the last published One Wales review report prepared in May 2023.

Background: Angioimmunoblastic T-cell lymphoma (AITL) is a rare and often aggressive form of peripheral T-cell lymphoma. Signs and symptoms include generalised lymphadenopathy, skin rash, arthritis, polyclonal hypergammaglobulinemia and autoimmune conditions such immune thrombocytopenia. Typical frontline therapy is CHOP-like (cyclophosphamide, doxorubicin, vincristine, and prednisolone) chemotherapy, followed by BEAM (carmustine [BCNU], etoposide, cytosine arabinoside [Ara-C] and melphalan) conditioned autograft. AITL patients commonly relapse, and not all patients are eligible for BEAM conditioned autograft. Clinicians in Wales therefore considered there was an unmet need for the subset of relapsed or refractory patients not suitable or unfit for BEAM. This medicine was therefore considered suitable for assessment via the One Wales Medicines process.

Current One Wales decision: The subcutaneous formulation of azacitidine is supported for use for this indication.

Licence status: Azacitidine is not licensed to treat progressive (relapsed or refractory) AITL; its use in this indication is off-label. AWTTC is not aware of any plans to pursue marketing authorisation of subcutaneous azacitidine for this indication at this time. The manufacturers of oral azacitidine are not pursuing a licence for this indication in the UK.

Guidelines: Updated European guidelines for systemic T-cell lymphomas (d'Amore et al. 2025) include angioimmunoblastic T-cell lymphoma (AITL) under the T follicular helper phenotype (TFHL) subgroup. For relapsed/refractory disease, the guideline notes that cyclosporin A, lenalidomide, and azacitidine have demonstrated efficacy. The guideline cites the phase III ORACLE trial as supportive of azacitidine's potential role in selected patients with TFHL.

Licensed alternative medicines or Health Technology Assessment advice for alternative medicines: No new medicines or Health Technology Assessment advice reported.

Effectiveness: AWTTC conducted a literature search in October 2025 to find new evidence for the use of azacitidine for the treatment of progressive AITL. The search excluded articles published before 2024, articles that reviewed evidence previously presented in AWTTC's first Evidence Summary Report (2020), and conference abstracts.

The search identified one open-label, randomised, phase 3 study (ORACLE) which evaluated oral azacitidine compared with standard therapy in adults with relapsed or refractory TFHL. The study's results were previously reported in the last review from a conference abstract and have now been verified in a peer-reviewed publication. Oral azacitidine was associated with prolonged overall survival and a favourable safety profile compared with standard care. However, it did not meet the primary outcome of the study, progression-free survival, this may be due to the study being underpowered. No papers for subcutaneous azacitidine were identified in the literature search.

Safety: Safety analyses from the ORACLE trial indicated a more favourable profile for azacitidine. Grade 3–4 adverse events occurred in 76% of patients receiving azacitidine versus 98% in the standard therapy group (gemcitabine, bendamustine or romidepsin), serious adverse events occurred in 26% versus 44% of patients respectively. The most common grade 3 or worse events were haematologic toxicities, infection and gastrointestinal toxicities. Haematologic toxicity was reported in 67% of azacitidine-treated patients compared with 93% in the standard therapy arm. Infection rates were lower with azacitidine (19% versus 33%), while gastrointestinal events were slightly higher (12% versus 2%). Treatment-related deaths occurred in two patients (one endocarditis and one candidiasis) in the azacitidine group and three in the standard therapy group (one heart failure, one COVID-19 and one cause unknown).

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

Budget impact: The original Evidence Status Report estimated an eligible population of approximately five patients per year in Wales. Since the last review in 2023, real-world outcome data provided by clinicians working in Wales indicate that five patients have received treatment in south Wales. The current price of generic azacitidine has significantly decreased under the All Wales Drug Contract. Specifically, azacitidine 100 mg subcutaneous 1 ml vial injection is now priced at [confidential text removed], whereas the original budget impact calculations were based on a price of [confidential text removed]. This change will result in a significant reduction in the budget impact for this treatment.

Impact on health and social care services: No new impact data have been provided, though we consider the impact of this medicine to be minimal.

Patient outcome data: Five patients from South Wales have received azacitidine for relapsed or refractory AITL spanning a data period of two to five years. [confidential text removed]
Clinicians note the limited usage of this treatment in Wales but would value its continued availability through One Wales when treatment is required.

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 the AWTTC website. 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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