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

Azacitidine for the treatment of progressive angioimmunoblastic T-cell lymphoma (OW16)

September 2021

ONE WALES INTERIM COMMISSIONING DECISION

Azacitidine for the treatment of progressive angioimmunoblastic T-cell lymphoma

Date of original advice: July 2020
Date of review: July 2021

The following Interim Pathways Commissioning Group (IPCG) recommendation has been endorsed by health board Chief Executives.

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

Azacitidine is not licensed to treat this indication and is therefore off-label. Each provider organisation must ensure all internal governance arrangements are completed before this medicine is prescribed.

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 advice will be reviewed after 2 years or earlier if new evidence becomes available.

Clinician responsibility
Clinicians will be obliged to collect and monitor patient outcomes. Evidence of clinical outcomes will be taken into consideration when reviewing the One Wales Interim Commissioning decision.

Health board responsibility
Health boards will take responsibility for implementing One Wales Interim Commissioning decisions and ensuring that a process is in place for monitoring clinical outcomes.

One Wales advice promotes consistency of access across NHS Wales.

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 and stopping criteria:

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 Interim Commissioning 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.

This is a summary of new evidence available and patient outcome data collected, to inform the 2021 review

Background
Angioimmunoblastic T-cell lymphoma (AITL) is a rare and often aggressive form of peripheral T-cell lymphoma (PTCL)[1,2]. Front line treatment is usually cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP)-like chemotherapy followed by BEAM (carmustine [BCNU], etoposide, cytosine arabinoside [Ara-C] and melphalan) conditioned autograft[1]. AITL has very high relapse rates and there is no clear treatment pathway for relapsed/refractory AITL if the patient is not fit or suitable for BEAM conditioned autograft. Clinicians in Wales consider there is an unmet need and have identified a cohort of patients who could benefit from this treatment. This medicine was therefore considered suitable for assessment via the One Wales process.

Current One Wales Interim Decision
Using the agreed starting and stopping criteria, azacitidine can be made available within NHS Wales for the treatment of progressive angioimmunoblastic T-cell lymphoma. July 2020[3].

Licence status
Azacitidine for progressive AITL is off-label.

Guidelines
There have been no new relevant guidelines or updates to existing guidelines identified.

Licensed alternative medicines/Health Technology Appraisal advice for alternative medicines
Azacitidine for treating relapsed or refractory angioimmunoblastic T-cell lymphoma has been proposed for consideration by NICE (NICE ID3864). There is no expected publication date currently.

Efficacy/Effectiveness
No new clinical trials were identified in the repeat literature search. The ORACLE study (Efficacy and Safety of Oral Azacitidine Compared to Investigator's Choice Therapy in Patients With Relapsed or Refractory AITL; NCT03593018) is on-going and due to be completed in December 2021[4].

Safety
No relevant safety analyses were identified in the repeat literature search.

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

Budget impact
Based on the patient numbers reported, it is likely that the budget impact for the last 12 months is lower than estimated in the original evidence status report. Clinical experts estimated five patients eligible for treatment with azacitidine per year. This lower treated case number may in part be due to the ongoing COVID-19 pandemic. Treatment duration was estimated to be six cycles in the original evidence status report. In the original evidence status report it was noted that the treatment duration of six months was subject to uncertainty due to the range of treatment lengths described in the case series by Lemonnier et al[2]. Under the current start/stop criteria patients are reviewed at three cycles then again after 12 months to consider whether there is continued clinical benefit for the patient and no evidence of disease progression[3].
[CONFIDENTIAL DATA REMOVED]

Impact on health and social care services
The impact on the service remains minimal.

Patient outcome data
[CONFIDENTIAL DATA REMOVED]

References

1. British Committee for Standards in Haematology. Guidelines for the Management of Mature T-cell and NK-cell Neoplasms (Excluding cutaneous T-cell Lymphoma). 2013. Available at: https://b-s-h.org.uk/media/2895/t-nhl-guideline-3-8-13-updated-with-changes-accepted-v1-rg.pdf. Accessed Jun 2021.
2. Lemonnier F, Dupuis J, Sujobert P et al. Treatment with 5-azacytidine induces a sustained response in patients with angioimmunoblastic T-cell lymphoma. *Blood.* 2018;132(21):2305-2309.
3. All Wales Therapeutics and Toxicology Centre. One Wales Interim Commissioning Decision. Azacitidine for the treatment of progressive angioimmunoblastic T-cell lymphoma. Jul 2020. Available at: https://www.awttc.org/pams/current-one-wales-interim-commissioning-decisions. Accessed Jun 2021.
4. The Lymphoma Academic Research Organisation, and Celgene. NCT03593018: Efficacy and Safety of Oral Azacitidine Compared to Investigator's Choice Therapy in Patients With Relapsed or Refractory AITL. Apr 2021. Available at: https://clinicaltrials.gov/ct2/show/NCT03593018. Accessed Jun 2021.