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

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

July 2020

ONE WALES INTERIM COMMISSIONING DECISION

Azacitidine for the treatment of progressive angioimmunoblastic T-cell lymphoma

Date of advice: July 2020

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 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 General Medical Council 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.

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.

One Wales Interim Commissioning Process
Interim Pathways Commissioning Group (IPCG) summary of decision rationale

Medicine: **azacitidine**
Indication: **treatment of progressive angioimmunoblastic T-cell lymphoma (AITL)**
Meeting date: **18th May 2020**

Criteria	IPCG opinion
Clinical effectiveness	IPCG notes that the clinical effectiveness evidence is from a case series of 12 patients and two case studies. There are no published comparisons between azacitidine and its main comparator as suggested by clinical experts in Wales, bendamustine. There is some evidence to suggest that bendamustine may be associated with more haematological toxicities when compared to azacitidine There are no randomised control trials of azacitidine to treat AITL, results of an ongoing trial using oral azacitidine (currently unlicensed) are expected in 2022. IPCG considers that the limited information provided demonstrated some evidence of clinical benefit.
Cost-effectiveness	IPCG notes that no cost effectiveness studies have been undertaken. There is insufficient information available to provide cost effectiveness analyses.
Budget impact	IPCG considers that the clinical estimate of patient numbers reported is reasonably accurate. IPCG acknowledges that budget impact estimates are subject to uncertainty. There is particular uncertainty around number of treatment cycles of azacitidine and differences in adverse event costs between azacitidine and its comparator. IPCG acknowledged that there will be a proportion of patients who respond to treatment with azacitidine and may continue on treatment for more than 6 months.
Other factors	IPCG notes that there is an ongoing clinical trial in the UK for the use of unlicensed oral azacitidine for the treatment of AITL. IPCG considers that entry into a clinical trial would be the preferred option for eligible patients within this cohort. This will be incorporated in to the start/stop criteria.
Final recommendation	IPCG recommends that azacitidine is made available for the treatment of progressive angioimmunoblastic T-cell lymphoma (AITL). This recommendation is subject to the development of appropriate start/stop criteria
Summary of rationale	There is some evidence to suggest that azacitidine is clinically effective for the treatment of angioimmunoblastic T-cell lymphoma and may be associated with greater tolerability in a predefined cohort of patients.