Grŵp Strategaeth Meddyginiaethau Cymru Gyfan
All Wales Medicines Strategy Group

One Wales Medicines Assessment Group Recommendation
Venetoclax (Venclyxto®) 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) as an alternative to intensive chemotherapy (OW32).

Date of advice: 02 December 2025
AWTTC reference number: OW32

Using the agreed starting and stopping criteria venetoclax (Venclyxto®) with azacitidine can be made available within NHS Wales 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) as an alternative to intensive chemotherapy.

The risks and benefits of the off-label use of venetoclax (Venclyxto®) with 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.

There is a simple discount patient access scheme (PAS) for venetoclax and an All Wales Drug Contract (AWDC) for azacitidine.

This recommendation has been endorsed by the All Wales Medicines Strategy Group (AWMSG) and ratified by Welsh Government.

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 Medicines Assessment decision.

Health board responsibility
Health boards will take responsibility for implementing One Wales Medicines Assessment Group decisions and ensuring that a process is in place for monitoring clinical outcomes

One Wales advice assists consistency of access across NHS Wales.

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

Starting and stopping criteria for the treatment 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) as an alternative to intensive chemotherapy.

Developed in collaboration with the haematological cancer services, Cardiff and Vale University Health Board.

Starting criteria:
Patients must satisfy all the following criteria. Treatment may be considered in adults (aged 18 years and above) who:

- Have relapsed or refractory AML, this includes patients with confirmed molecular measurable residual disease (MRD) relapse and patients who have previously received an allogenic haematopoietic stem cell transplant
- Have received at least one prior line of treatment with intensive chemotherapy
- Are ineligible for treatment with gilteritinib (patient does not have a FLT3-activating mutation)
- Are unsuitable for further intensive salvage chemotherapy
- the patient has not previously demonstrated refractoriness (failure to achieve a meaningful disease response after 3 cycles of venetoclax-containing therapy) or intolerance to venetoclax-based therapy

A list of precautions is included in the Summary of Product Characteristics (SmPC)[1,2].

Patients who satisfy the eligibility criteria will be prescribed venetoclax with azacitidine following consultation with the patient and/or carer after consideration of potential adverse effects, cautions, contraindications and an explanation of alternative treatment options. This consultation should be recorded in the patient's notes.

Venetoclax dosing begins with 100 mg orally on day 1, increasing to 200 mg on day 2, 400 mg on day 3, then reduced back down to 100 mg daily on day 4 and thereafter. Azole antifungals start on day 4. In cases of drug-induced cytopenia, treatment cycles may be shortened to 14–21 days. If neutrophil counts normalise, the azole antifungal may be stopped and venetoclax increased to 400 mg daily.

Venetoclax is metabolised by enzyme cytochrome P450 3A4 (CYP3A4), therefore co-administration with strong CYP3A4 inhibitors such as azole antifungals necessitates a dose reduction to mitigate toxicity[1]. Venetoclax 400 mg orally daily is only used in patients who cannot take azole antifungals or who achieve remission with normal blood counts and no longer require antifungal prophylaxis.

Azacitidine is administered at 75 mg/m² via subcutaneous injection into the upper arm, thigh or abdomen on days 1–7, though in practice it is often given on days 1–5 and 8–9 to avoid weekend hospital visits.

Treatment typically continues until disease relapse. Patients who are medically fit and achieve remission may proceed to allogeneic HSCT, at which point venetoclax and azacitidine are stopped.

Recommended modifications to manage adverse reactions are provided in the SmPC[1,2].

Monitoring:

- Daily full blood count for 2 weeks of cycle 1 then 1-2 times a week
- Urea and electrolytes
- Liver function tests
- Clinical evaluation of side effects, refer to SmPC
- Bone marrow biopsy prior to starting treatment and repeated at day 21-28 to assess initial response and guide need for GCSF

Tumour burden assessment, must be performed for all patients. Tumour lysis syndrome can occur as early as 6 to 8 hours after the first dose of venetoclax and at each subsequent dose increase. To reduce this risk, a gradual dose escalation is recommended, along with prophylactic hydration and anti-hyperuricemic therapy before initiating treatment.

Nausea and vomiting are frequent adverse effects of azacitidine, patients should be administered prophylactic anti-emetic therapy for the first 2 cycles of azacitidine treatment.

Treatment with venetoclax and azacitidine can be associated with neutropenia, thrombocytopenia and febrile neutropenia. Supportive care such as antibiotics and/or antipyretics for management of infection/fever and GCSF for neutropenia should be provided based on individual patient characteristics, treatment response and according to the current clinical guidelines[1,2].

This list is not exhaustive. Any other monitoring should be in accordance with the SmPC for venetoclax and azacitidine[1,2].

Stopping criteria:

- evidence of clinically significant disease progression or symptomatic deterioration as agreed in the MDT
- objective clinical response has not been achieved following 3 cycles of treatment
- consolidation of treatment response with allogenic HSCT or donor lymphocyte infusion, this would generally occur after 2-3 cycles of treatment with venetoclax and azacitidine.
- toxicity; dosing reduction may be considered, follow the guidance in the SmPC.
- patient request

Other considerations:

- AWTTC patient information leaflets on understanding unlicensed medicines in English and Welsh and an easy read format, these can be accessed here.
- It is important that outcomes are collected for this patient cohort and the outcomes will be reviewed by the One Wales Medicines Assessment Group after 12 months.
- Clinicians may wish to use one of the Cancer Research UK consent forms for SACT (Systemic Anti-Cancer Therapy) to help ensure your patient is fully informed when consenting to SACT.
- The Strategic Clinical Network for Cancer standard is that all patients receiving SACT should be given the All Wales Cancer Treatment Alert Card with the treating team being responsible for ensuring that the details of which treatment type and name is clearly indicated on the card and the patient is given supporting information and explanations. Further information can be found here: Systemic Anti-Cancer Therapies (SACT) - NHS Wales Executive

References

1. AbbVie Ltd. Summary of Product Characteristics: Venclyxto 100 mg film-coated tablets. 26 Feb 2025. Available at: https://www.medicines.org.uk/emc/product/10476/smpc. Accessed November 2025.
2. Zentiva. Summary of Product Characteristics: Azacitidine 25 mg/mL powder for suspension for injection. Available at: https://www.medicines.org.uk/emc/product/12470/smpc. Accessed November 2025.