azaCITIDine (Oral) Monotherapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
Maintenance treatment in adult patients with acute myeloid leukaemia (AML) who achieved complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following induction therapy with or without consolidation treatment and who are not candidates for, including those who choose not to proceed to, haematopoietic stem cell transplantation (HSCT).	C92	00818a	CDS 01/12/2023

* This is for post 2012 indications only.

Note: The oral formulation of azaCITIDine is not interchangeable with injectable azaCITIDine due to differences in the activity, exposure, dose and schedule of treatment.

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

azaCITIDine is taken orally on days 1-14 of a 28 day cycle and continued until no more than 15% blasts are observed in peripheral blood or bone marrow or until unacceptable toxicity occurs.

Day	Drug	Dose	Route	Cycle
1-14*	azaCITIDine	300mg	PO	Every 28 days
* In the case of disease relapse, with 5% to 15% blasts in peripheral blood or bone marrow, in conjunction with a clinical assessment, **an extension of the dosing schedule from 14 to 21 days of repeated 28-day cycles should be considered**. Dosing should not exceed 21 days during any 28-day period. Treatment should be discontinued if more than 15% blasts are observed in either the peripheral blood or bone marrow or at the physician's discretion.				
Oral azaCITIDine can be taken with or without food. The tablets should be swallowed whole with a glass of water at about the same time each day. They should not be split, crushed, dissolved or chewed.				
If a dose of is missed, or not taken at the usual time, the dose should be taken as soon as possible on the same day. Then, the next scheduled dose should be taken at the normal time the following day. Two doses should not be taken on the same day				
If a dose is vomited, another dose must not be taken on the same day. Instead return to the normal time of dose administration the following day.				

ELIGIBILITY:

- Indication as above
- ECOG 0-3
- Adequate organ function and bone marrow function
- Intermediate or poor cytogenetic risk

EXCLUSIONS:

- Hypersensitivity to azaCITIDine or any of the excipients
- Achieved CR/CRi following therapy with hypomethylating agents
- Pregnancy
- Breastfeeding

CAUTIONS:

- Any uncontrolled active infection

PRESCRIPTIVE AUTHORITY:

- The treatment plan must be initiated by a Consultant Haematologist working in the area of haematological malignancies

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Coagulation screen
- Virology screen - Hepatitis B virus (HBV) serology [HBV sAg, HBV sAb, HBV cAb], hepatitis C virus (HCV) serology, human immunodeficiency virus (HIV) serology, cytomegalovirus (CMV) serology [IgG] and additional screening as clinically indicated
  (See Regimen Specific Complications for information on Hepatitis B reactivation)

Regular tests:

- FBC every two weeks for first two cycles, every two weeks for two cycles after dose adjustment, and monthly thereafter (prior to start of subsequent treatment cycle)
- Renal and liver profile

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant

Haematological:

Table 1: Dose modification in haematological toxicity

Criteria*	Recommended action
Grade 4 neutropenia or Grade 3 neutropenia with fever	First occurrence • Interrupt treatment. Resume the treatment cycle at the same dose once neutrophils return to Grade 2 or lower • Use supportive care such as granulocyte colony stimulating factor (GCSF), as clinically indicated Occurrence in 2 consecutive cycles • Interrupt treatment. Resume the treatment cycle at a reduced dose of 200 mg after neutrophils return to Grade 2 or lower • If a patient continues to experience the toxicity after dose reduction, reduce the treatment duration by 7 days • If the toxicity continues or re-occurs after dose and schedule reduction, discontinue treatment • Use supportive care such as GCSF, as clinically indicated
Grade 4 thrombocytopenia or Grade 3 thrombocytopenia with bleeding	First occurrence • Interrupt treatment. Resume the treatment cycle at the same dose once platelets return to Grade 2 or lower Occurrence in 2 consecutive cycles • Interrupt treatment. Resume the treatment cycle at a reduced dose of 200 mg after platelets return to Grade 2 or lower • If a patient continues to experience the toxicity after dose reduction, reduce the treatment duration by 7 days • If the toxicity continues or re-occurs after dose and schedule reduction, discontinue treatment

* Grade 1 is mild, Grade 2 is moderate, Grade 3 is severe, Grade 4 is life-threatening. Toxicity grades are in accordance with National Cancer Institute Common Terminology Criteria for Adverse Events Version 4.3 (NCI-CTCAE v4.3)

Renal and Hepatic Impairment:

Table 2: Dose modification in renal and hepatic impairment

Renal impairment	Hepatic impairment		
No dose adjustment is required	**Grade**	**Parameter(s)**	**Dose Modification**
	Mild	Total bilirubin ≤ ULN and AST > ULN, **or** Total bilirubin 1-1.5 × ULN and any AST	No dose adjustment is required
	Moderate	Total bilirubin >1.5-3 x ULN	Patients should be monitored more frequently for adverse events and appropriate dose adjustment should be made as per Table 1 and Table 3
	Severe	Total bilirubin >3 x ULN	

Management of adverse events:

Table 3: Dose Modification for Adverse Events

Criteria*	Recommended action
Grade 3 or higher nausea, vomiting or diarrhoea	• Interrupt treatment. Resume the treatment cycle at the same dose once toxicity has resolved to Grade 1 or lower • Use supportive care such as anti-emetic therapy and treat diarrhoea at the onset of symptoms • If event re-occurs, interrupt dose until resolved to Grade 1 or lower and reduce the dose to 200 mg • If a patient continues to experience the toxicity after dose reduction, reduce the treatment duration by 7 days If the toxicity continues or re-occurs after dose and schedule reduction, discontinue treatment
Other Grade 3 or higher non-haematological events	• Interrupt treatment and provide medical support according to local recommendations. Resume the treatment cycle at the same dose once toxicity has resolved to Grade 1 or lower • If the toxicity re-occurs, interrupt treatment until resolved to Grade 1 or lower and reduce dose to 200 mg • If a patient continues to experience the toxicity after dose reduction, reduce the treatment duration by 7 days • If the toxicity continues or re-occurs after dose and schedule reduction, discontinue treatment

* Grade 1 is mild, Grade 2 is moderate, Grade 3 is severe, Grade 4 is life-threatening. Toxicity grades are in accordance with National Cancer Institute Common Terminology Criteria for Adverse Events Version 4.3 (NCI-CTCAE v4.3)

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL

- As outlined in NCCP Classification Document for Systemic Anti Cancer Therapy (SACT) Induced Nausea and Vomiting- Available on the NCCP website

azaCITIDine: Moderate to high (**Refer to local policy and premedications below)**

For information:

Within NCIS regimens, antiemetics have been standardised by Medical Oncologists and Haemato-oncologists. Information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for Inclusion in NCIS (Medical Oncology) - Available on the NCCP website
- NCCP Supportive Care Antiemetic Medicines for Inclusion in NCIS (Haemato-oncology) - Available on the NCCP website

PREMEDICATIONS:

- Patients are to be treated with an anti-emetic 30 minutes prior to each dose of azaCITIDine for the first 2 treatment cycles. Anti-emetic prophylaxis may be omitted after 2 cycles, if there has been no nausea and vomiting.

OTHER SUPPORTIVE CARE:

- G-CSF support may be required **(Refer to local policy)**
- Anti-diarrhoeal therapy may be required **(Refer to local policy)**
- Anti-viral prophylaxis may be required **(Refer to local policy)**
- Anti-fungal prophylaxis may be required **(Refer to local policy)**
- Proton pump Inhibitor **(Refer to local policy)**
- Women of childbearing potential have to use effective contraception during and up to 6 months after treatment. Men have to use effective contraception during and up to 3 months after treatment

ADVERSE EFFECTS:

- Please refer to the relevant Summary of Product Characteristics for details.

REGIMEN SPECIFIC COMPLICATIONS:

- **Hepatitis B Reactivation:** Patients should be tested for both HBsAg and HBcoreAb as per local policy. If either test is positive, such patients should be treated with anti-viral therapy. **(Refer to local infectious disease policy).** These patients should be considered for assessment by hepatology.

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for information.

REFERENCES:

1. Wei A, et al. Oral Azacitidine Maintenance Therapy for Acute Myeloid Leukaemia in First Remission. N Engl J Med 2020; 383: 2526-2537. Available at: https://www.nejm.org/doi/full/10.1056/NEJMoa2004444
2. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Antiemesis Version 2.2024 – September 27, 2024. Accessed January 2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf
3. Azacitidine (Onureg®) Summary of Product Characteristics. Accessed Oct 2024. Available at: https://www.ema.europa.eu/en/documents/product-information/onureg-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	08/12/2023		Dr Eibhlin Conneally
2	04/04/2025	Regimen reviewed.Updated exclusions section. Addition of	Dr Nina Orfali

		Cautions section. Updated renal and hepatic dose modifications table. Updated regimen in line with NCCP standardisation.	

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.