Decitabine Monotherapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
Treatment of adult patients aged 65 years and above with newly diagnosed de novo or secondary acute myeloid leukaemia (AML), according to the WHO classification, who are not candidates for standard induction chemotherapy.	C92	00231a	ODMS

*This applies to post 2012 indications

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.

Decitabine is administered daily for 5 days, followed by a rest period of 23 days (28-day treatment cycle) for a **minimum** of 4 cycles. A complete or partial remission may take longer than 4 cycles to be obtained. Treatment should be continued as long as the patient shows response, continues to benefit or exhibits stable disease, i.e. in the absence of overt progression.
If after 4 cycles, the patient's haematological values have not returned to pre-treatment levels or if disease progression occurs, the patient may be considered to be a non-responder and alternative therapeutic options should be considered.

Facilities to treat anaphylaxis MUST be present when systemic anti-cancer therapy (SACT) is administered.

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1-5	Decitabine	20mg/m^2	IV	in 0.9% sodium chloride over **60 minutes**	Every 28 days for four cycles
Final concentration of decitabine should be 0.15 to 1.0 mg/ml. If a dose is missed, treatment should be resumed as soon as possible. **Note: Each vial of decitabine 50mg contains 0.5mmol potassium and 0.29mmol sodium**					

ELIGIBILITY:

- Indication as above
- ECOG 0-2

EXCLUSIONS:

- Hypersensitivity to decitabine or any of the excipients
- Breast Feeding

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PRESCRIPTIVE AUTHORITY:

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

TESTS:

Baseline tests:

- Blood, renal and liver profile
- Bone marrow examination and cytogenetics as baseline

Regular tests:

- Blood prior to each cycle or as clinically indicated
- Renal and liver profile prior to each cycle
- Bone marrow examination after 4 cycles and thereafter at 6 monthly intervals as indicated.

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:

Treatment may be delayed at the discretion of the prescribing consultant if the patient experiences myelosuppression-associated complications such as those described below:

- Febrile neutropenia (temperature >38.5°C and ANC<1.0x10^9/L).
- Active viral, bacterial or fungal infection.
- Haemorrhage (gastrointestinal (GI), genitourinary, pulmonary with platelets <25x10^9/L or any CNS haemorrhage).

Treatment with decitabine may be resumed once these conditions have improved or have been stabilised with adequate treatment (anti-infective therapy, transfusions, or growth factors).

In clinical studies, approximately one-third of patients receiving decitabine required a dose-delay. Dose reduction is not recommended.

Renal and Hepatic Impairment:

Table 1: Dose modification of decitabine in renal and hepatic impairment

Renal impairment	Hepatic impairment
Studies in patients with renal impairment have not been conducted. Caution should be exercised in the administration of decitabine to patients with severe renal impairment (CrCl<30ml/min).	Studies in patients with hepatic impairment have not been conducted. If worsening hepatic function occurs, patients should be carefully monitored.

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SUPPORTIVE CARE:

EMETOGENIC POTENTIAL

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

Decitabine: Low **(Refer to local policy).**

For information:
Within NCIS regimens, antiemetics have been standardised by the 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: None usually required.

OTHER SUPPORTIVE CARE:

- Supportive treatments include administration of prophylactic antibiotics and/or growth factor support (e.g. G-CSF) for neutropenia and transfusions for anaemia or thrombocytopenia **(Refer to local policy).**
- Decitabine may have moderate influence on the ability to drive and use machines. Patients should be advised that they may experience undesirable effects such as anaemia during treatment. Therefore, caution should be recommended when driving a car or operating machines.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

- **Myelosuppression:** Myelosuppression and complications of myelosuppression, including infections and bleeding that occur in patients with AML may be exacerbated with decitabine treatment. Complete blood and platelet counts should be performed regularly, as clinically indicated and prior to each treatment cycle. In the presence of myelosuppression or its complications, treatment may be interrupted or supportive measures instituted (Reference other supportive care above).
- **Cardiac disease:** Patients with a history of severe congestive heart failure (CHF) or clinically unstable cardiac disease were excluded from clinical studies and therefore the safety and efficacy of decitabine in these patients has not been established. Cases of cardiomyopathy with cardiac decompensation, in some cases reversible after treatment discontinuation, dose reduction or corrective treatment, have been reported in the postmarketing setting. Patients, especially those with cardiac disease history, should be monitored for signs and symptoms of heart failure.
- **Respiratory, thoracic and mediastinal disorders:** Cases of interstitial lung disease (ILD) without signs of infectious aetiology have been reported in patients receiving decitabine. Careful assessment of

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patients with an acute onset or unexplained worsening of pulmonary symptoms should be performed to exclude ILD. If ILD is confirmed, appropriate treatment should be initiated.

- **Differentiation syndrome:** Cases of differentiation syndrome (similar to retinoic acid syndrome associated with all-trans retinoic acid) have been reported in patients receiving decitabine). Treatment with high-dose IV corticosteroids and haemodynamic monitoring should be considered at first onset of symptoms or signs suggestive of differentiation syndrome. Temporary discontinuation of decitabine should be considered until resolution of symptoms and if resumed, caution is advised.

DRUG INTERACTIONS:

- No formal clinical drug interaction studies with decitabine have been conducted.
- Potential for a drug-drug interaction with other agents which are also activated by sequential phosphorylation and/or metabolised by enzymes implicated in the inactivation of decitabine (e.g. cytidine deaminase).
- Current drug interaction databases should be consulted for more information.

REFERENCES:

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2. Kantarjian H, Issa J-P, Rosenfeld CS et al. Decitabine improves patient outcomes in myelodysplatic syndromes: results of a phase III randomized study. Cancer 2006;106:1794-80.
3. DACOGEN® (decitabine) 50 mg, powder for concentrate for solution for infusion – Change in the recommendations for diluting reconstituted Dacogen solution. Available at: http://www.hpra.ie/docs/default-source/Safety-Notices/important-safety-information---dacogen-(decitabine).pdf?sfvrsn=0
4. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V5 2023. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf
5. Decitabine (DACOGEN®) Summary of product characteristics EMA. Last updated: 20/07/2021. Accessed: May 2023. Available at: https://www.ema.europa.eu/en/documents/product-information/dacogen-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	2/01/2014	Initial Draft	Dr Helen Enright
2	12/01/2016	Inserted statement on need to report adverse reactions in Adverse Effects/Regimen specific complications	Dr Helen Enright
3	11/09/2017	Updated with new NCCP regimen template and updated concentration range of the final product for administration. This has been narrowed from '0.1 mg/ml-1.0 mg/ml' to '0.15 mg/ml-1.0 mg/ml' to comply with European Pharmacopoeia	Dr Helen Enright

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4	25/11/2019	Reviewed. Standardised treatment table. Updated adverse events.	Dr Helen Enright
5	08/08/2023	Reviewed. Updated emetogenic potential and adverse events section.	Dr Helen Enright
5a	24/06/2025	Updated emetogenic potential section with added links.	NCCP

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

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