High Dose Cytarabine Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Consolidation chemotherapy for the treatment of patients with Acute Myeloid Leukaemia (AML)	C92	00365a	Hospital

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.

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

Treatment is administered on Day 1, 3 and 5.
Treatment with cycle 2 may proceed on count recovery.

Day	Drug	Dose	Route	Diluent and rate
1,3,5	Cytarabine	3000mg/m^2 **AM**	IV infusion	500mls NaCl 0.9% over 4 hours
1,3,5	Cytarabine	3000mg/m^2 **PM (12 hours after start of AM infusion)**	IV infusion	500mls NaCl 0.9% over 4 hours

ELIGIBILITY:

- Patients < 60 years
- ECOG status 0-2

EXCLUSIONS:

- Hypersensitivity to cytarabine or any of the excipients
- Breast feeding
- Pregnancy

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
- Glucose
- Coagulation screen (Activated Partial Thromboplastin time [APTT], Prothrombin time [PT], fibrinogen level)

Regular tests:

- FBC, renal and liver profile
- Glucose daily or as clinically indicated
- Coagulation profile: APTT, PT, fibrinogen level at least twice weekly or more frequently as clinically 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
- **Dose reductions not generally undertaken in this regimen**
- **Note: Dose modification required in renal impairment (Ref Table 1)**

Renal and Hepatic Impairment:

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

Drug	Renal Impairment		Hepatic Impairment
Cytarabine	**CrCl (ml/min)**	**Dose**	If bilirubin >34micromol/L, give 50% dose. Escalate doses in subsequent cycles in the absence of toxicity.
	>60	100%	
	46-60	60%	
	31-45	50%	
	<30	CI	

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Moderate **(Refer to local policy)**.

PREMEDICATIONS:

To prevent a chemical induced conjunctivitis developing with cytarabine, prednisoLONE eye drops (e.g. Pred Mild®) 1-2 drops per eye 4 hourly during waking hours prior to cytarabine and continued 5 days post treatment should be considered.

OTHER SUPPORTIVE CARE:

- Proton pump Inhibitor **(Refer to local policy)**
- Anti-viral prophylaxis **(Refer to local policy)**
- Anti-fungal prophylaxis **(Refer to local policy)**

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:** Cytarabine is a potent bone marrow suppressant. Patients receiving this drug must be under close medical supervision and, during induction therapy, should have leucocyte and platelet counts performed daily. Bone marrow examinations should be performed frequently after blasts have disappeared from the peripheral blood**.**
- **Neurotoxicity:** This may occur in patients treated with high dose cytarabine. Assess cerebellar function prior to each cytarabine dose. The risk of neurotoxicity is enhanced in the presence of renal impairment. Ensure that dose of cytarabine is adjusted in renal impairment (Ref Table 1).
- **Cytarabine syndrome:** Treatment with cytarabine may cause a 'Cytarabine Syndrome' characterised by flu-like symptoms, skin rash and occasionally chest pain.

DRUG INTERACTIONS:

- Current drug interaction databases should be consulted for more information.

REFERENCES:

1. Mayer RJ, et al. Intensive post remission chemotherapy in patients with acute myeloid leukaemia. New England Journal of Medicine. 1994; 331:896-903.
2. Burnett A.K et al. Optimization of Chemotherapy for Younger Patients with Acute Myeloid Leukaemia: Results of the medical Research Council AML15 Trial. J Clin Oncol. 2013:31(27):3360-8.
3. AML 17 Version 8.0 (October 2012) https://trials.cardiff.ac.uk/aml/17/web/files/new5/AML%2017%20Protocol%20V8.0%20October%202012.pdf
4. Hanoun, Maher et al. "Intensified cytarabine dose during consolidation in adult AML patients under 65 years is not associated with survival benefit: real-world data from the German SAL-AML registry." *Journal of cancer research and clinical oncology*, 10.1007/s00432-022-04356-9. 28 Sep. 2022, doi:10.1007/s00432-022-04356-9
5. Dosage Adjustment for Cytotoxics in Renal Impairment January 2009; North London Cancer Network . Dosage Adjustment for Cytotoxics in Hepatic Impairment January 2009; North London Cancer Network.
6. 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
7. Cytarabine Summary of Product Characteristics. Last updated: April 2021 Accessed Feb 2023 . Available at : https://www.medicines.ie/medicines/cytarabine-20-mg-ml-solution-for-injection-or-infusion-31768/spc

Version	Date	Amendment	Approved By
1	03/07/2017		Dr Eibhlin Conneally, Dr Catherine Flynn
2	30/09/2019	Biannual review	Dr Eibhlin Conneally, Dr Catherine Flynn
3	08/08/2023	Reviewed. Eligibility criteria updated.	Dr Eibhlin Conneally, Dr Catherine Flynn

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.