DA (50/100) (3+8) Course 2 Induction Therapy (AML-17)

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Induction chemotherapy regimen for the treatment of patients with de novo or secondary Acute Myeloid Leukaemia (AML)	C92	00360a	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.

Order of Admin	Day	Drug	Dose	Route	Diluent and Rate
1	1,3, and 5 (3 doses)	DAUNOrubicin	50mg/m^2	IV Bolus	Slow IV push via side arm NaCl 0.9% infusion (A central line is preferred)
2	1 to 8 Inclusive	Cytarabine	100mg/m^2 **AM**	IV infusion	100mls NaCl 0.9% over 30 mins
3	1 to 8 Inclusive	Cytarabine	100mg/m^2 **PM (12 hours after start of AM infusion)**	IV infusion	100mls NaCl 0.9% over 30 mins
Lifetime cumulative dose of DAUNOrubicin is 550mg/m^2 **In establishing the maximal cumulative dose of an anthracycline, consideration should be given to the risk factors [i] and to the age of the patient**					

ELIGIBILITY:

- Indication as above
- ECOG status 0-2
- Age <70 generally. Patients older than this may be eligible if intensive therapy is considered a suitable option
- Patients who have completed a Course 1 Induction Therapy and achieved remission

EXCLUSIONS:

- Hypersensitivity to DAUNOrubicin, cytarabine, or any of the excipients
- LVEF <45% (The treatment of patients with baseline LVEF <45% should only be initiated at the discretion of the treating consultant)
- Breast feeding

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, LDH, Uric acid
- Coagulation profile: APTT, PT, fibrinogen
- MUGA or ECHO as clinically indicated
- Chest X-ray
- Pregnancy test

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
- MUGA or ECHO 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 induction regimens

Renal and Hepatic Impairment:

Table 1: Dose modifications based on renal and hepatic impairment

Drug	Renal Impairment		Hepatic Impairment	
DAUNOrubicin	**Creatinine (micromol/L)**	**Dose**	**Bilirubin (micromol/L)**	**Dose**
	<105	100%	<20	100%
	105-265	75%	20-50	75%
	>265	50%	>50	50%
Cytarabine	No dose reduction necessary		If bilirubin >34micromol/L, give 50% dose. Escalate doses in subsequent cycles in the absence of toxicity.	

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

DAUNOrubicin: Moderate (**Refer to local policy).**
Cytarabine: Low (**Refer to local policy).**

PREMEDICATIONS: Not usually required.

OTHER SUPPORTIVE CARE:

- Tumour lysis syndrome prophylaxis. If at high risk consider rasburicase **(Refer to local policy)**
- Proton pump Inhibitor**(Refer to local policy)**
- Anti-viral prophylaxis **(Refer to local policy)**
- Anti-fungal prophylaxis **(Refer to local policy)**
- Mouth/oral care **(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:** This is a very myelosuppresive regimen. 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.

DAUNOrubicin

- **Cardiotoxicity:** Extreme caution should be exercised when using daunorubicin in patients with cardiac disorders or in the elderly. Cardiotoxicity if it occurs is likely to be heralded by either a persistent tachycardia, shortness of breath, swelling of feet and lower limbs or by minor changes in the electrocardiogram and for this reason an electrocardiographic examination should be made at regular intervals during the treatment. Cardiotoxicity usually appears within 1 to 6 months after initiation of the therapy. It may develop suddenly and not be detected by routine ECG. It may be irreversible and fatal but responds to treatment if detected early.

  Extravasation: DAUNOrubicin is a potent vesicant. Give through the side arm of a fast flowing infusion ideally through a central access line to avoid/minimise the risk of extravasation.

Cytarabine

- **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:

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2. Krens S D, Lassche,Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. Lancet Onco/2019; 20:e201-08. https://doi.org/10.1016/S1470-2045(19)30145-7
3. Dosage Adjustment for Cytotoxics in Renal Impairment January 2009; North London Cancer Network .
4. Dosage Adjustment for Cytotoxics in Hepatic Impairment January 2009;North London Cancer Network.

5. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V4 2022. 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
6. Cerubidin® Summary of Product Characteristics. Last updated: 28/06/19. Accessed May 2022 Available at https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA0540-096-001_28062019145807.pdf
7. Cytarabine Summary of Product Characteristics. Last updated: 18/08/21. Accessed May 2022 Available at: https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA0822-200-002_18082021114137.pdf

Version	Date	Amendment	Approved By
1	03/07/2017		Dr Eibhlin Conneally, Dr Catherine Flynn
2	30/09/2019	Inclusion of tallman lettering for DAUNOrubicin	Dr Eibhlin Conneally, Dr Catherine Flynn
3	25/11/2022	Reviewed. Updated eligibility section. Updated emetogenic potential.	Dr Eibhlin Conneally, Dr Catherine Flynn

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

[ii]Cardiotoxicity is a risk associated with anthracycline therapy that may be manifested by early (acute) or late (delayed) effects.

Risk factors for developing anthracycline-induced cardiotoxicity include:

high cumulative dose, previous therapy with other anthracyclines or anthracenediones
- prior or concomitant radiotherapy to the mediastinal/pericardial area
- pre-existing heart disease
- concomitant use of other potentially cardiotoxic drugs

In establishing the maximal cumulative dose of an anthracycline, consideration should be given to the risk factors above and to the age of the patient.