FLAG:Ida 8mg/m^2 Therapy[i]

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	*Reimbursement Status
Induction chemotherapy regimen for the treatment of patients with de novo, secondary Acute Myeloid Leukaemia (AML), or biphenotypic leukaemia.	C92	00362a	Hospital
Treatment of patients with high blast count (>10%) Myelodysplastic Syndrome	D46	00362b	Hospital
Salvage regimen for patients with relapsed/refractory acute leukaemia	C91 C92	00362c	Hospital

**If the reimbursement status is not defined[ii], the indication has yet to be assessed through the formal HSE reimbursement process.*

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.

Treatment is administered as described in the treatment table below. Further cycles, up to a maximum of 3, can be given at the discretion of the treating consultant.

Day	Drug	Dose	Route	Diluent and rate
0-6 inclusive	[a]G-CSF	5microgram/kg	SC	Round to full syringe
1, 2,3,4,5, inclusive	[b]Fludarabine	30mg/m^2	IV infusion	100mls 0.9% NaCl over 30 mins
1,2,3,4,5, inclusive	Cytarabine	2000mg/m^2	IV infusion	500mls 0.9% NaCl over 4 hours **Commence 4 hours after start of Fludarabine infusion**
3, 4, and 5 inclusive	[c]IDArubicin	8mg/m^2	IV Bolus	Slow bolus in free running 0.9% NaCl drip over 5-10 min
[a] G-CSF may be continued at the discretion of the prescribing Consultant				
[b]All patients who have received fludarabine should receive irradiated blood products (lifetime recommendation).				
[c]Check patient's lifetime anthracycline exposure prior to prescribing IDArubicin There is no established maximum cumulative lifetime dose for IDArubicin. **Due consideration should be given to the risk factors [iii] and to the age of the patient**				

ELIGIBILTY:

- ECOG status 0-2
- Age <60 generally. May be used in older patients if deemed fit for intensive therapy by prescribing consultant
- In patients with relapsed/refractory disease cumulative anthracycline exposure should be determined to ensure that the patient has not reached the maximum doses

EXCLUSIONS:

- Hypersensitivity to cytarabine, fludarabine, IDArubicin 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
- Uric acid, LDH, Glucose
- Coagulation profile (Activated Partial Thromboplastin time (APTT), Prothrombin time (PT), fibrinogen level)
- MUGA or ECHO as clinically indicated
- Virology screen -Hepatitis B (HBsAg, HBcoreAb)
  All patients should be tested for both HBsAg and HBcoreAb as per local policy. If either test is positive, such patients should be treated with Lamivudine 100 mg/day orally, for the entire duration of chemotherapy and for six months afterwards. Such patients should also be monitored with frequent liver function tests and hepatitis B virus DNA at least every two months. If the hepatitis B virus DNA level rises during this monitoring, management should be reviewed with an appropriate specialist with experience managing hepatitis and consideration given to halting chemotherapy.

Regular tests:

- FBC, renal and liver profile daily or as clinically indicated
- Uric acid, 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

Renal and Hepatic Impairment:

Table 1: Dose modifications based on renal and hepatic impairment

Drug	Renal Impairment		Hepatic Impairment	
Cytarabine	**GFR (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	Contraindicated		
Fludarabine	**Creatinine Cl (ml/min)**	**Dose**	No dose changes recommended	
	>70	100%		
	30-70	50%		
	<30	Contraindicated		
IDArubicin	**Creatinine Cl (ml/min)**	**Dose (7)**	**Bilirubin (micromol/L)**	**Dose**
	≥50	100%	<40	100%
	10-50	75%	40-85	50%
	<10	50%	>85	Omit

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:

- Tumour lysis syndrome prophylaxis **(Refer to local policy)**
- Proton pump Inhibitor**(Refer to local policy)**
- PJP prophylaxis **(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**.** Fludarabine, cytarabine and IDArubicin are all myelosuppressive agents. Caution is required in pre-treated patients, those with a history of opportunistic infections and the elderly.

Fludarabine:

- **Hepatitis B reactivation:** The immunosuppression associated with fludarabine may increase the risk of re-activation of hepatitis B. If the patient is HBsAg positive consult local hepatologist as per local policy.

Cytarabine:

- **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 fever, flu-like symptoms, skin rash and occasionally chest pain.

Idarubicin:

- **Cardiotoxicity**: Cardiac toxicity may occur, manifested by cardiac failure, arrhythmias or cardiomyopathies, either during therapy or several weeks later. The cumulative dose associated with cardiotoxicity is not known, Cardiac function monitoring must be particularly strict in patients receiving high cumulative doses and in those with risk factors. However, cardiotoxicity with IDArubicin may occur at lower cumulative doses whether or not cardiac risk factors are present.
- **Extravasation**: IDArubicin is a potent vesicant. Give through the side arm of a fast flowing infusion to avoid/minimise the risk of extravasation.

DRUG INTERACTIONS:

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

ATC CODE:

Cytarabine	-	L01BC01
Fludarabine	-	L01BB05
IDArubicin	-	L01DB06

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Version	Date	Amendment	Approved By
1	05/09/2018		Dr Kamal Fadalla

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

[i] This is an unlicensed indication for the use of Fludarabine in Ireland. Patients should be informed of this and consented to treatment in line with the hospital's policy on the use of unlicensed medication and unlicensed or "off label" indications. Prescribers should be fully aware of their responsibility in communicating any relevant information to the patient and also ensuring that the unlicensed or "off label" indication has been acknowledged by the hospital's Drugs and Therapeutics Committee, or equivalent, in line with hospital policy.

[ii] ODMS – Oncology Drug Management System
CDS – Community Drug Schemes (CDS) including the High Tech arrangements of the PCRS community drug schemes
Further details on the Cancer Drug Management Programme is available at;
http://www.hse.ie/eng/services/list/5/cancer/profinfo/medonc/cdmp/

[iii] 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.