Rota code: HROTA448	Issue date: June 2025	Written by: Steve Hill	Authorised by: Consultant:	Page: 1 of 5
Version no. 1.0	Valid until: Next Review	Checked by (Pharmacist) S.Dhadda	Clinical Nurse Specialist: ELENA TEJERO GDS	Reference: NHSE Policy: URN2320

NHS University Hospitals Birmingham NHS Foundation Trust

Arsenic Trioxide/ATRA with Idarubicin Induction—High Risk APML:

MRN: Ward/Unit:

Name:

DOB: Consultant:

Address:

NHS No:

Hb		Na+		Alb		Height	
WBC		K+		AlKP		Weight	
Plt		Urea		ALT		BSA	
Neuts		Cr		Bili		Date	
		GFR		TSH		Allergies :	
		Ca		T4			
		Mg		Cortisol			
Recorded by		Date					

Indication: Newly Diagnosed High Risk APML

Single cycle only. To be given up to 60 days (8.5 weeks) or until unacceptable toxicity

Funding status: Blueteq required

Blueteq ID:

Emetogenic potential: highly emetogenic

Extravasation classification:
Vesicant—idarubicin
Non-Vesicant—Arsenic Trioxide

Treatment intent: Curative

Cycle frequency and duration: Up to 60 days

Cycle number: 1

Day No. Date	DRUG or ELECTROLYTE	CALCULATION	DOSE	IV FLUIDS	VOL. MLS.	ROUTE/FLOW RATE	SPECIAL DIRECTIONS/ ADMINISTRATION DETAILS	DRUG ADMINISTRATION Sig.	Sig.	TIME	Pharmacy
Week 1, D1	**IDARUBICIN**	12mg/m^2		Sodium Chloride 0.9%	100ml	20 mins	If no central line, must be given by IV bolus down the side arm of a fast running drip				
Week 1, D1	**ARSENIC TRIOXIDE**	0.3mg/kg		Sodium Chloride 0.9%	250ml	IV Infusion over 2 hours*					
Week 1, D2	**ARSENIC TRIOXIDE**	0.3mg/kg		Sodium Chloride 0.9%	250ml	IV Infusion over 2 hours*					
Week 1, D3	**IDARUBICIN**	12mg/m^2		Sodium Chloride 0.9%	100ml	20 mins	If no central line, must be given by IV bolus down the side arm of a fast running drip				
Week 1, D3	**ARSENIC TRIOXIDE**	0.3mg/kg		Sodium Chloride 0.9%	250ml	IV Infusion over 2 hours*					
Week 1, D4	**ARSENIC TRIOXIDE**	0.3mg/kg		Sodium Chloride 0.9%	250ml	IV Infusion over 2 hours*					
Week 1, D5	**IDARUBICIN**	12mg/m^2		Sodium Chloride 0.9%	100ml	20 mins	~~Check with prescriber if WCC < 1^9/L~~ If no central line, must be given by IV bolus down the side arm of a fast running drip				
Week 1, D5	**ARSENIC TRIOXIDE**	0.3mg/kg		Sodium Chloride 0.9%	250ml	IV Infusion over 2 hours*					

Prescriber sig.....name..... Date: ..... Nurse sig..... name..... Date..... Pharmacist sig..... ..name..... Date.....

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Week 2, D1	**ARSENIC TRIOXIDE**	0.25mg/kg		Sodium Chloride 0.9%	250ml	IV Infusion over 2 hours*					
Week 2, D4	**ARSENIC TRIOXIDE**	0.25mg/kg		Sodium Chloride 0.9%	250ml	IV Infusion over 2 hours*					
Week 3, D1	**ARSENIC TRIOXIDE**	0.25mg/kg		Sodium Chloride 0.9%	250ml	IV Infusion over 2 hours*					
Week 3, D4	**ARSENIC TRIOXIDE**	0.25mg/kg		Sodium Chloride 0.9%	250ml	IV Infusion over 2 hours*					
Week 4, D1	**ARSENIC TRIOXIDE**	0.25mg/kg		Sodium Chloride 0.9%	250ml	IV Infusion over 2 hours*					
Week 4, D4	**ARSENIC TRIOXIDE**	0.25mg/kg		Sodium Chloride 0.9%	250ml	IV Infusion over 2 hours*					
Week 5, D1	**ARSENIC TRIOXIDE**	0.25mg/kg		Sodium Chloride 0.9%	250ml	IV Infusion over 2 hours*					
Week 5, D4	**ARSENIC TRIOXIDE**	0.25mg/kg		Sodium Chloride 0.9%	250ml	IV Infusion over 2 hours*					

Prescriber sig.....name..... Date: ..... Nurse sig..... name..... Date..... Pharmacist sig..... ..name..... Date.....

Arsenic Trioxide/ATRA with Idarubicin Induction—High Risk APML:

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DOB: Consultant:

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		Ca		T4			
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Treatment intent: Curative

Cycle frequency and duration: Up to 60 days

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Day No. Date	DRUG or ELECTRO-LYTE	CALCULATION	DOSE	IV FLUIDS	VOL. MLS.	ROUTE/FLOW RATE	SPECIAL DIRECTIONS/ ADMINISTRATION DETAILS	DRUG ADMINISTRATION Sig.	Sig.	TIME	Pharmacy
Week 6, D1	**ARSENIC TRIOXIDE**	0.25mg/kg		Sodium Chloride 0.9%	250ml	IV Infusion over 2 hours*					
Week 6, D4	**ARSENIC TRIOXIDE**	0.25mg/kg		Sodium Chloride 0.9%	250ml	IV Infusion over 2 hours*					
Week 7, D1	**ARSENIC TRIOXIDE**	0.25mg/kg		Sodium Chloride 0.9%	250ml	IV Infusion over 2 hours*					
Week 7, D4	**ARSENIC TRIOXIDE**	0.25mg/kg		Sodium Chloride 0.9%	250ml	IV Infusion over 2 hours*					
Week 8, D1	**ARSENIC TRIOXIDE**	0.25mg/kg		Sodium Chloride 0.9%	250ml	IV Infusion over 2 hours*					
Week 8, D4	**ARSENIC TRIOXIDE**	0.25mg/kg		Sodium Chloride 0.9%	250ml	IV Infusion over 2 hours*					

Prescriber sig.....name..... Date: ..... Nurse sig..... name..... Date..... Pharmacist sig..... ..name..... Date.....

Arsenic Trioxide/ATRA with Idarubicin Induction—High Risk APML:

Proceed rules, valid within 96 hours (FBC must be conducted at least twice weekly throughout induction):

Drug	Neuts	Platelets	Renal	Hepatic
Arsenic Trioxide	N/A	N/A	GFR ≥ 30mL/min: 100% dose GFR < 30ml/min: Consider 50% dose	Mild/moderate impairment (Child-Pugh Stage A or B): 100% dose. Use with caution due to risk of hepatotoxicity Severe impairment (Child-Pugh Stage C): Consider 50% dose If persistent increase in bilirubin, AST/ALT, or ALP > 5 X ULN despite ATRA Interruption, pause Arsenic Trioxide
Idarubicin	N/A	N/A	GFR ≥ 30mL/min: 100% dose GFR < 30ml/min: 67% dose	Bilirubin 45-86 µmol/L: 50% dose Bilirubin >86 µmol/L: Not recommended
Tretinoin (ATRA)	N/A	N/A	GFR < 50mL/min: Reduce dose to 25mg/m2 daily, in 2 divided doses	Clinical decision due to lack of information. 25mg/m^2 daily, in 2 divided doses is advised by the product license. An increase in bilirubin, AST/ALT, or ALP > 5 X ULN. Temporarily withhold ATRA.

Medications to be prescribed on PICS	
Anti-emetics	**Supportive medication**
Ondansetron 8mg BD PO/IV on days 1, 3 and 5 only (same day as idarubicin) Metoclopramide 10mg TDS PO/IV on days 1-5, then 10mg TDS PO/IV PRN.	Tretinoin (ATRA) 45mg/m^2 PO in two equal divided doses (round to nearest 10mg). To continue until complete remission or a maximum of 60 days treatment. Allopurinol 300mg OD (consider rasburicase if high TLS risk) Omeprazole 20mg OD while platelets are < 50 x 10^9/L or as clinically indicated

Arsenic Trioxide Administration

*Arsenic trioxide must be administered intravenously over 1-2 hours. The infusion duration may be extended up to 4 hours if vasomotor reactions (e.g. flushing, dizziness, tachycardia) are observed.

Cardiac Monitoring

Cardiac Monitoring:
Perform a 12-lead ECG. For corrected QT interval (QTc) >500 msec, take immediate corrective measures and reassess the QTc with serial ECGs before using arsenic. Refer to SPC for further information. ECGs indicated pre-treatment then at least twice weekly during induction.
Provide continuous monitoring for patients with risk factors for QTc prolongation or torsades de pointes.
Maintain serum potassium >4mmol/L and magnesium >0.74mmol/L. Pre-existing electrolyte abnormalities should be corrected.
If possible discontinue any medicines that are known to prolong QT.

Idarubicin-related cardiomyopathy was reported in 5% of patients who received cumulative intravenous doses of 150 to 290 mg/m2. A baseline ECHO should be performed prior to initiation.

Arsenic Trioxide/ATRA with Idarubicin Induction—High Risk APML:

Other Information

Differentiation Syndrome:

Differentiation syndrome can present with leukocytosis, fever, pulmonary infiltrates (hypoxia) and/or weight gain. Temporarily discontinue arsenic/ATRA and initiate dexamethasone 10mg IV BD for a minimum of 3 days. Discuss with attending haematology consultant and refer to SPC for further advice

Dose modifications for toxicity:

Arsenic Trioxide:

- Potential toxicities— Differentiation Syndrome, QTc prolongation, Hepatotoxicity
- For toxicities ≥ grade 3 interrupt/stop treatment. Resume only after toxicity resolution or recovery to baseline. Resume at 50% of the pre-interruption dose. If no toxicity recurrence within 7 days, consider escalation to 100% dose. Stop treatment if toxicity re-occurs.
- If stopped due to hepatotoxicity, this can be resumed at 50% of the previous dose for 7 days, when bilirubin, AST/ALT or ALP are reduced to < 4 x ULN. In absence of worsening of the previous toxicity, arsenic trioxide can be resumed at full dosage

Tretinoin (ATRA):

- Potential toxicities—Differentiation Syndrome, Pseudotumour cerebri, Hepatotoxicity
- When symptoms and clinical condition improve, resume ATRA at 50% previous dose during the first 4 days after the disappearance of differentiation syndrome, amelioration of pseudotumour cerebri or when bilirubin, AST/ALT or ALP are reduced to < 4 x ULN. In absence of worsening of the previous toxicity, ATRA can be resumed at full dosage.
- In case of toxicity recurrence, stop drug indefinitely during induction therapy.

Coagulopathy:

APTT, prothrombin time, thrombin time, fibrinogen level and platelet count should be checked at least twice daily in the early stages of treatment.
Aim for fibrinogen levels of approximately >1—1.5g/L using cryoprecipitate/FFP. Avoid elevated levels due to increased thrombotic risk.
Ideally aim for platelets > 50 x 10^9/L until morphological remission confirmed.
Avoid routine use of heparin or anti-fibrinolytics (e.g. tranexamic acid).

Drug Interactions:

Contraindicated combinations

- Vitamin A - risk of symptoms suggestive of hypervitaminosis A for daily doses greater than 10,000 IU.
- Oral retinoids e.g. isotretinoin, acitretin, bexarotene
- Tetracyclines – increased intracranial hypertension risk (pseudotumour cerebri)
- Antifibrinolytics (e.g. tranexamic acid) – risk of fatal thrombotic complications

CYP3A4 inducers (e.g. rifampicin, carbamazepine) and inhibitors (e.e. voriconazole, clarithromycin) can affect tretinoin metabolism and are ideally best avoided. Combination with strong CYP3A4 inhibitors may trigger toxicity. A dose reduction could be considered if necessary.

If possible discontinue any medicines that are known to prolong QT.