Regimen Reference Order

LEUK – APML4 Maintenance (APL)

ARIA: LEUK - [APML4 Maintenance]

Planned Course: **8 Cycles (1 cycle = 90 days)**
Indication for Use: **Acute Promyelocytic Leukemia; High Risk**

CVAD: At Provider's Discretion

Proceed with treatment if:
Days 1, 30, and 60

- ***ANC equal to or greater than 1 x 10^9/L AND Platelets equal to or greater than 100 x 10^9/L***

Dose adjustments are made to target an ANC of 1 to 2 x 10^9/L

- **Contact Leukemia/BMT (L/BMT) Physician if parameters not met**

SEQUENCE OF MEDICATION ADMINISTRATION

Pre-treatment Requirements

Drug	Dose	CCMB Administration Guideline
Not Applicable		

Treatment Regimen*
LEUK – APML4 – Maintenance (APL)

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
Maintenance starts 3 to 4 weeks after completion of LEUK – APML4 Consolidation Cycle 2 (APL)		
Days 1 to 14		
VESANOID® (ATRA)	45 mg/m^2/day (to nearest 10 mg)	Orally divided twice daily on **Days 1 to 14 only** Take with food. Swallow whole **(Self-administered at home)**
Days 15 to 90		
methotrexate	5 to 15 mg/m^2 (to nearest 2.5 mg)	Orally **once weekly** on an empty stomach in the evening on **Days 15, 22, 29, 36, 43, 50, 57, 64, 71, 78 and 85** **(Self-administered at home)**
mercaptopurine	50 to 90 mg/m^2	Orally once daily on an empty stomach Do not crush or chew **(Self-administered at home)**

****See Appendix A – Maintenance (high risk group) dosing schema***

all-trans retinoic acid (VESANOID®) available dosage strength: 10 mg capsule
Classification: Non-Cytotoxic, Hazardous

methotrexate available dosage strength: 2.5 mg tablet
Classification: Cytotoxic, Hazardous

mercaptopurine (Purinethol®) available dosage strength: 50 mg tablet
Classification: Cytotoxic, Hazardous

******* Note: ATRA = all-trans retinoic acid = tretinoin = VESANOID® *******
Not to be confused with isotretinoin (ACCUTANE®, EPURIS® or CLARUS®)

In the event of an infusion-related hypersensitivity reaction, refer to the **'Hypersensitivity Reaction Standing Order'**

REQUIRED MONITORING

Baseline
- CBC, serum creatinine, urea, sodium, potassium, calcium, magnesium, phosphate, ALK, AST, ALT, total bilirubin, LDH, albumin, uric acid, cholesterol, triglycerides, INR, PTT and fibrinogen as per Physician Orders

Day 30
- CBC and full biochemistry

Day 60
- CBC and full biochemistry

Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
valACYclovir	500 mg	Orally twice daily

DISCHARGE INSTRUCTIONS

- Patients should be instructed to monitor for and report any treatment related side effects. This may include edema, abdominal pain, diarrhea, nausea, vomiting, dizziness, headache or cough
- Instruct patient to report shortness of breath or signs/symptoms of arrhythmias (dizziness, palpitations or fainting)
- VESANOID® (ATRA) has potential for significant drug-drug interactions. Patients should notify clinic prior to starting any new medication
- Avoid grapefruit and grapefruit juice, Seville oranges (i.e. orange marmalade) and starfruit
- mercaptopurine should not be taken with milk or citrus based products. Cow's milk in particular, contains high concentrations of xanthine oxidase which inactivates mercaptopurine
- Remind patient to take valACYclovir (shingles prophylaxis) at home
- Reinforce safe handling precautions of medications, blood and body fluids for 48 hours after completion of chemotherapy

ADDITIONAL INFORMATION

- **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated aggressively
- **Renal dysfunction:** patients with creatinine clearance less than 30 mL/minute may require dose reduction
- **APL differentiation syndrome (DS)** is defined as unexplained fever, dyspnea, pleural and/or pericardial effusion, pulmonary infiltrates, renal failure, hypotension and unexplained weight gain greater than 5 kg. Severe DS is defined as 4 or more of these signs or symptoms and moderate DS is defined as 2 or more signs and symptoms. dexamethasone 10 mg IV twice daily should be initiated
- **Leukocytosis** may develop after treatment initiation. Patients can be treated with hydroxyurea 500 mg orally four times daily for WBC 10-50 x 10^9/L or 1000 mg orally four times daily for WBC greater than 50 x 10^9/L. Discontinue hydroxyurea when WBC is less than 10 x 10^9/L
- **Transient, mild headache** may occur several hours after ATRA ingestion
- **Hypervitaminosis A syndrome** has been observed with ATRA, and may include xeroderma, lip and mouth dryness, cheilitis, rash, edema, nausea, vomiting and bone pain
- **Benign or idiopathic intracranial hypertension** (pseudotumour cerebri) may occur with an onset of about 3-17 days of ATRA therapy
- **Venous and arterial thrombosis** is a risk during the first month of ATRA treatment
- **Hepatitis B Reactivation:** All patients should be tested for HBsAg and HBcAb. If either test is positive, such patients should be treated with tenofovir 300 mg/day orally for the entire duration of the chemotherapy and for six months afterwards. The patients should also be monitored with frequent liver enzymes 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

Appendix A

Maintenance (high risk group) dosing schema

Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
VESANOID® (ATRA) 45 mg/m^2/day orally divided twice daily	■	■	■	■	■	■	■	■	■	■	■	■	■	■																
methotrexate 5 to 15 mg/m^2/week															■							■							■	
mercaptopurine 50 to 90 mg/m^2/day															■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■

Day	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60
VESANOID® (ATRA) 45 mg/m^2/day orally divided twice daily																														
methotrexate 5 to 15 mg/m^2/week						■							■							■							■			
mercaptopurine 50 to 90 mg/m^2/day	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■

Day	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90
VESANOID® (ATRA) 45 mg/m^2/day orally divided twice daily																														
methotrexate 5 to 15 mg/m^2/week				■							■							■							■					
mercaptopurine 50 to 90 mg/m^2/day	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■

Key: ■ indicates that this medication will be administered on this day