Regimen Reference Order – LYMP – escalated BEACOPP

ARIA: LYMP – [escalated BEACOPP]

Planned Course: **Every 21 days up to a maximum of 4 cycles**
Indication for Use: **Hodgkin Lymphoma**

CVAD: At Provider's Discretion (VESICANT INVOLVED)

Proceed with treatment if:

Day 1

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

Day 8

- ***Blood work results not required to proceed with treatment***
  - **Contact Hematologist if parameters not met**

Note: Hepatitis B serology results must be reviewed in accordance with CCMB Policy Hepatitis B Monitoring for Oncology and Hematology Patients

SEQUENCE OF MEDICATION ADMINISTRATION

Pre-treatment Requirements

Drug	Dose	CCMB Administration Guideline
Instruct patient to start vigorous oral pre-hydration (600-900 mL) the morning of cyclophosphamide treatment **(Self-administered at home)**		
allopurinol	300 mg	Orally once daily for 10 days to begin 3 days prior to Cycle 1 **(Self-administered at home)** Only patients at risk of tumor lysis syndrome will be prescribed allopurinol Note: allopurinol should not be prescribed beyond 10 days unless under the direction of the hematologist. See *Additional Information*

Treatment Regimen – LYMP – escalated BEACOPP

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
Day 1		
predniSONE	40 mg/m^2	Orally once in the morning with food **(Self-administered at home)**
aprepitant	125 mg	Orally 1 hour pre chemotherapy
ondansetron	16 mg	Orally 30 minutes pre chemotherapy
normal saline	500 mL	IV over 1 hour (Pre hydration)
DOXOrubicin	35 mg/m^2	IV push over 10 minutes

mesna	250 mg/m^2	IV in normal saline 50 mL over 15 minutes immediately prior to cyclophosphamide
cyclophosphamide	1250 mg/m^2	IV in normal saline 500 mL over 2 hours **Alert: start of cyclophosphamide infusion will be considered "Hour 0"*
etoposide	200 mg/m^2	IV in normal saline 1000 mL over 2 hours from "Hour 2" to "Hour 4" *Use non-DEHP bags and non-DEHP administration sets*
mesna	250 mg/m^2	IV in normal saline 50 mL over 15 minutes at "Hour 4"
mesna	500 mg/m^2	Orally with juice or soft drink at "Hour 6" **(Self-administered at home)** **Nursing Alert: Inform patient time to take dose*
ondansetron	8 mg	Orally once 30 minutes before bedtime procarbazine dose **(Self-administered at home)**
procarbazine	100 mg/m^2 (see Table 1 procarbazine Dosing)	Orally once at bedtime on an empty stomach Swallow whole **(Self-administered at home)**
Drug	**Dose**	**CCMB Administration Guideline**
Days 2 and 3		
predniSONE	40 mg/m^2	Orally once daily in the morning with food **(Self-administered at home)**
Establish primary solution 500 mL of: normal saline		
aprepitant	80 mg	Orally 1 hour pre-chemotherapy
etoposide	200 mg/m^2	IV in normal saline 1000 mL over 2 hours *Use non-DEHP bags and non-DEHP administration sets*
ondansetron	8 mg	Orally once daily 30 minutes pre-chemotherapy **(Self-administered at home)**
procarbazine	100 mg/m^2 (see Table 1 procarbazine Dosing)	Orally once daily at bedtime on an empty stomach Swallow whole **(Self-administered at home)**
Days 4 to 7		
predniSONE	40 mg/m^2	Orally once daily in the morning with food **(Self-administered at home)**
ondansetron	8 mg	Orally once daily 30 minutes pre-chemotherapy **(Self-administered at home)**
procarbazine	100 mg/m^2 (see Table 1 procarbazine Dosing)	Orally once daily at bedtime on an empty stomach Swallow whole **(Self-administered at home)**

Day 8		
predniSONE	40 mg/m^2	Orally once in the morning with food **(Self-administered at home)**
Establish primary solution 500 mL of: normal saline		
vinCRIStine	1.4 mg/m^2; maximum dose 2 mg	IV in normal saline 25 mL over 2 to 3 minutes by gravity infusion
hydrocortisone	100 mg	IV in normal saline 50 mL over 15 minutes
bleomycin	10 units/m^2	IV in normal saline 50 mL over 10 minutes
Days 9 to 14		
predniSONE	40 mg/m^2	Orally once daily in the morning with food **(Self-administered at home)**
predniSONE available dosage strengths: 5 mg and 50 mg tablets **procarbazine available dosage strength: 50 mg capsule** **Classification: Cytotoxic, Hazardous**		

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

REQUIRED MONITORING

Hepatitis B serology

- Hepatitis B surface antigen and Hepatitis B core antibody (drawn within preceding 5 years)

Cardiac monitoring

- Left Ventricular Ejection Fraction (LVEF) monitoring is recommended
  - At baseline, and
  - Post 2 cycles of escalated BEACOPP (i.e. after total of 4 cycles of chemotherapy) and as clinically indicated

Pulmonary Function Tests (PFTs)

- Post 2 cycles of escalated BEACOPP (i.e. after total of 4 cycles of chemotherapy) and as clinically indicated

All Cycles

Days 1 and 8 (results not required for treatment on Day 8)

- CBC, type and screen, serum creatinine, urea, electrolytes, liver enzymes, LDH, total bilirubin, uric acid, albumin and glucose as per Physician Orders

Twice weekly between Days 8 to 21

- CBC, type and screen, serum creatinine, urea, electrolytes, liver enzymes, LDH, total bilirubin, uric acid, albumin and glucose as per Physician Orders
- Clinic assessment for transfusion needs, infections, mucositis, hydration and electrolyte abnormalities

Prior to each cycle, the hematologist will assess for potential dose level modifications for subsequent cycles

Dose Levels (adapted from Cancer Care Ontario):

	Dose Level 1 (*Standard BEACOPP*)	**Dose Level 2**	**Dose Level 3**	**Dose Level 4**	**Dose Level 5 (*Escalated BEACOPP)***
DOXOrubicin	25 mg/m^2	35 mg/m^2	35 mg/m^2	35 mg/m^2	35 mg/m^2
cyclophosphamide	650 mg/m^2	800 mg/m^2	950 mg/m^2	1100 mg/m^2	1250 mg/m^2
etoposide	100 mg/m^2	125 mg/m^2	150 mg/m^2	175 mg/m^2	200 mg/m^2

Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
pegfilgrastim (brand name specific)	6 mg	Subcutaneous once on Day 9 **Alert: pegfilgrastim to be given as a single dose once per chemotherapy cycle no sooner than 24 hours after chemotherapy*
omeprazole	20 mg	Orally once daily
valACYclovir	500 mg	Orally once daily
sulfamethoxazole-trimethoprim	800 mg/160 mg	Orally twice daily on Saturdays and Sundays
metoclopramide	10 – 20 mg	Orally every 4 hours as needed for nausea and vomiting
At prescriber's discretion, when indicated:		
nystatin suspension	100,000 units (1 mL)	Orally swish and swallow four times daily
ANUSOL-HC® ointment	Apply sparingly to affected area	Apply topically twice daily

DISCHARGE INSTRUCTIONS

- Patients should be instructed to contact their cancer team immediately if symptoms of hypersensitivity reactions occur after discharge
- Ensure patient receives pegfilgrastim supply if patient is self-administering at home
- Instruct patient to:
    - Self-administer "Hour 6" of mesna on Day 1 by mixing the contents of the mesna syringe in juice (not grapefruit) or soft drink. If patient vomits within 2 hours of taking "Hour 6" mesna, they should be advised to contact their cancer team. Patient may require intravenous hydration
    - Maintain oral intake of 2000 mL (8 glasses) of fluid daily at home
    - Report hematuria or dysuria
    - Empty bladder every 2 hours while awake and at bedtime for 24 hours after each dose of cyclophosphamide
    - Notify clinic prior to starting any new medication. Medications in this regimen have potential for drug-drug interactions
    - Avoid grapefruit and grapefruit juice, Seville oranges (i.e. orange marmalade) and starfruit
    - Avoid alcohol and certain foods which contain tyramine (e.g. deli meats, aged cheese) for at least 7 days before starting, during, and for at least 7 days after completing procarbazine as they may interact with procarbazine
- predniSONE and procarbazine are cancer therapies in this treatment regimen. Remind patient to take prednisone and procarbazine at home
- Remind patient to take support medications at home
- Reinforce applicable safe handling precautions of medications, blood and body fluids for 48 hours after completion of chemotherapy

ADDITIONAL INFORMATION

- All cycles of this regimen must be prescribed by a CCMB hematologist, due to the high risk of Grade 3 or 4 toxicities
- bleomycin is associated with pulmonary toxicity
- Due to the risk of reactivation of Hepatitis B virus (HBV) while on this treatment regimen, prescriber must adhere to CCMB Policy ***Hepatitis B Monitoring for Oncology and Hematology Patients*** for ordering and interpreting HBV serology and prescribing antiviral prophylaxis
- valACYclovir (shingles prophylaxis) and sulfamethoxazole-trimethoprim (*Pneumocystis jirovecii* pneumonia prophylaxis) continue while on treatment and for 3 months after discontinuation of treatment
- Unless patient was taking allopurinol for gout or other reasons unrelated to the patient's underlying lymphoma, allopurinol should not be prescribed with cycle 2 and onwards unless directed by hematologist
- Cumulative DOXOrubicin dose (including prior ABVD therapy) should be calculated and should not exceed 450 mg/m^2
- predniSONE, ondansetron and procarbazine will be dispensed by CCMB Pharmacy
- Due to the duration of treatment, administration site restrictions may be in place for Day 1 only

procarbazine Dosing – LYMP – escalated BEACOPP regimen

In the LYMP – escalated BEACOPP regimen, procarbazine should be dosed at 100 mg/m^2/day on Days 1 to 7 of the 21-day cycle. Because procarbazine is only available as a 50 mg capsule, there is limited flexibility in delivering the appropriate daily dose. As such, the dosing schedule may require alternating daily doses to ensure an appropriate dose over the course of the cycle.

While the Medical Oncology Manager (ARIA®) application is used for order entry and a specific regimen for the LYMP – escalated BEACOPP regimen is available, the dose calculations required for procarbazine are too complex to build into the ARIA-based regimen. Manual calculation and verification of procarbazine dosing is required and dosing instructions will require manual entry in ARIA under a "take as directed" prescription for procarbazine.

Here are a few steps to assist with dose calculation of procarbazine in the LYMP – escalated BEACOPP regimen.

1) Determine the total <u>cycle</u> dose of procarbazine:

100 mg/m^2/day x 7 days = 700 mg/m^2/cycle

BSA (m^2) x 700 mg/m^2/cycle = _____ mg of procarbazine required for the cycle.

Round this procarbazine amount to the nearest 50 mg.

<u>Example</u>: BSA = 2.2 m^2

700 mg/m^2/cycle x 2.2 m^2 = 1540 mg, or **1550 mg of procarbazine required for cycle**

2) Determine the <u>alternating dose schedule</u> for procarbazine:

A total of 7 days of procarbazine will be required. It is most likely that alternating doses (e.g. 250 mg, 200 mg, 150 mg orally daily) will be required to administer the appropriate procarbazine dose over the 7-day course. Please refer to Table 1 procarbazine Dosing for suggested dosing schedules, according to BSA.

3) Enter procarbazine daily dosing instructions into ARIA:

The procarbazine prescription as part of the LYMP – escalated BEACOPP regimen in ARIA should be a "take as directed" prescription, "Pick-Up – Internal". Once the doses of procarbazine have been determined, the administration instructions and dispensing quantity for procarbazine should be manually entered into ARIA.

<u>Example:</u>

Rx: procarbazine 50 mg capsule – Take as directed

<u>Administration instructions:</u>
Take 200 mg (four x 50 mg capsules) orally at bedtime on Days 1, 3, 5, and 7. Take 250 mg (five x 50 mg capsules) orally at bedtime on Days 2, 4, and 6. Take procarbazine on an empty stomach 30 minutes after ondansetron. Please refer to medication calendar for further details.
Refrain from alcohol and tyramine-containing foods for at least 7 days before starting, during, and for at least 7 days after completing procarbazine prescription.

<u>Quantity:</u> 31 x 50 mg capsules

Table 1
procarbazine Dosing – Sorted by Descending BSA

BSA (m^2)	Total Cycle procarbazine Dose	Number of days with **250 mg** dose	Number of days with **200 mg** dose	Number of days with **150 mg** dose	Number of days with **100 mg** dose
2.47-2.53	**1750 mg** (35 capsules)	7 (Days 1-7)	0	0	0
2.4-2.46	**1700 mg** (34 capsules)	6 (Days 1-6)	1 (Day 7)	0	0
2.33-2.39	**1650 mg** (33 capsules)	5 (Days 1, 2, 4, 5, 7)	2 (Days 3, 6)	0	0
2.25-2.32	**1600 mg** (32 capsules)	4 (Days 1, 3, 5, 7)	3 (Days 2, 4, 6)	0	0
2.18-2.24	**1550 mg** (31 capsules)	3 (Days 2, 4, 6)	4 (Days 1, 3, 5, 7)	0	0
2.11-2.17	**1500 mg** (30 capsules)	2 (Days 3, 6)	5 (Days 1, 2, 4, 5, 7)	0	0
2.04-2.10	**1450 mg** (29 capsules)	1 (Day 1)	6 (Days 2-7)	0	0
1.97-2.03	**1400 mg** (28 capsules)	0	7 (Days 1-7)	0	0
1.90-1.96	**1350 mg** (27 capsules)	0	6 (Days 1-6)	1 (Day 7)	0
1.83-1.89	**1300 mg** (26 capsules)	0	5 (Days 1, 2, 4, 5, 7)	2 (Days 3, 6)	0
1.75-1.82	**1250 mg** (25 capsules)	0	4 (Days 1, 3, 5, 7)	3 (Days 2, 4, 6)	0
1.68-1.74	**1200 mg** (24 capsules)	0	3 (Days 2, 4, 6)	4 (Days 1, 3, 5, 7)	0
1.61-1.67	**1150 mg** (23 capsules)	0	2 (Days 3, 6)	5 (Days 1, 2, 4, 5, 7)	0
1.54-1.60	**1100 mg** (22 capsules)	0	1 (Day 1)	6 (Days 2-7)	0
1.47-1.53	**1050 mg** (21 capsules)	0	0	7 (Days 1-7)	0
1.4-1.46	**1000 mg** (20 capsules)	0	0	6 (Days 1-6)	1 (Day 7)
1.33-1.39	**950 mg** (19 capsules)	0	0	5 (Days 1, 2, 4, 5, 7)	2 (Days 3, 6)
1.25-1.32	**900 mg** (18 capsules)	0	0	4 (Days 1, 3, 5, 7)	3 (Days 2, 4, 6)
1.18-1.24	**850 mg** (17 capsules)			3 (Days 2, 4, 6)	4 (Days 1, 3, 5, 7)