

Regimen Reference Order

LYMP – D-CBD (amyloidosis) (IV daratumumab)

ARIA: LYMP - [D-CBD (IV) amyloidosis]

Planned Course: Every 28 days until disease progression or unacceptable toxicity, up to a maximum of 2 years (24 cycles)

Indication for Use: Light Chain (AL) Amyloidosis

CVAD: At Provider's Discretion

Proceed with treatment if:

Day 1 ONLY

ANC equal to or greater than $1 \times 10^9/L$ AND Platelets equal to or greater than $75 \times 10^9/L$

❖ **Contact Hematologist if parameters not met**

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)		
montelukast	10 mg	Orally once daily in the morning starting the day before daratumumab to Day 4, Days 7 to 11, Days 14 to 18 and Days 21 to 25 of Cycle 1 Cycle 2 and onwards at the discretion of the physician (Self-administered at home) <i>*Nursing Alert: Notify physician if patient has not taken montelukast. montelukast is prescribed to prevent infusion reactions</i>

Treatment Regimen – LYMP – D-CBD (amyloidosis) (IV daratumumab)

Establish primary solution 500 mL of: normal saline		
Drug	Dose	CCMB Administration Guideline
Cycle 1		
cetirizine	10 mg	Orally 1 hour prior to daratumumab on Days 1, 2, 8, 15 and 22
acetaminophen	975 mg	Orally 1 hour prior to daratumumab on Days 1, 2, 8, 15 and 22
dexamethasone	16 mg	IV in normal saline 50 mL over 15 minutes 1 hour prior to daratumumab on Days 1, 2, 8, 15 and 22 <i>*Nursing Alert: daratumumab starts 1 hour after completion of dexamethasone</i>
bortezomib	1.3 mg/m ²	Subcutaneous injection once weekly on Days 1, 8, 15 and 22
Wait 1 hour after completion of IV pre-medication(s) before starting daratumumab		

daratumumab	8 mg/kg	<p>Slow infusion: IV in normal saline 500 mL on Days 1 and 2 following administration rates below:</p> <ul style="list-style-type: none"> • 0 to 60 minutes – 50 mL/hour • 60 to 120 minutes – 100 mL/hour • 120 to 180 minutes – 150 mL/hour • 180 minutes onwards – 200 mL/hour <p>Use 0.2 or 0.22 micron filter</p> <p><i>*Alert: Pharmacy to ensure final volume in bag = 500 mL</i></p> <p><i>*Nursing Alert: IV tubing is primed with daratumumab</i></p>
	16 mg/kg	<p>Rapid infusion: IV in normal saline 500 mL over 90 minutes on Days 8, 15, and 22: infuse 100 mL over 30 minutes, then infuse the remaining 400 mL over 60 minutes</p> <p>Use 0.2 or 0.22 micron filter</p> <p><i>*Alert: Pharmacy to ensure final volume in bag = 500 mL</i></p> <p><i>*Nursing Alert: IV tubing is primed with daratumumab</i></p>
cyclophosphamide	300 mg/m ² ; maximum dose 500 mg	Orally once daily in the morning on Days 1, 8, 15 and 22 Take with or without food. Swallow whole (Self-administered at home)
dexamethasone	4 mg	Orally once daily in the morning with food on Days 9, 16 and 23 (Self-administered at home)
Cycle 2		
dexamethasone	20 mg	Orally once daily in the morning with food on Days 1, 8, 15 and 22 (Self-administered at home)
cetirizine	10 mg	Orally 30 minutes prior to daratumumab on Days 1, 8, 15 and 22
acetaminophen	975 mg	Orally 30 minutes prior to daratumumab on Days 1, 8, 15 and 22
bortezomib	1.3 mg/m ²	Subcutaneous injection once weekly on Days 1, 8, 15 and 22
daratumumab	16 mg/kg	<p>Rapid infusion: IV in normal saline 500 mL over 90 minutes on Days 1, 8, 15, and 22: infuse 100 mL over 30 minutes, then infuse the remaining 400 mL over 60 minutes</p> <p>Use 0.2 or 0.22 micron filter</p> <p><i>*Alert: Pharmacy to ensure final volume in bag = 500 mL</i></p> <p><i>*Nursing Alert: IV tubing is primed with daratumumab</i></p>
cyclophosphamide	300 mg/m ² ; maximum dose 500 mg	Orally once daily in the morning on Days 1, 8, 15 and 22 Take with or without food. Swallow whole (Self-administered at home)
Cycles 3 to 6		
dexamethasone	20 mg	Orally once daily in the morning with food on Days 1, 8, 15 and 22 (Self-administered at home)
cetirizine	10 mg	Orally 30 minutes prior to daratumumab on Days 1 and 15
acetaminophen	975 mg	Orally 30 minutes prior to daratumumab on Days 1 and 15

bortezomib	1.3 mg/m ²	Subcutaneous injection once weekly on Days 1, 8, 15 and 22
daratumumab	16 mg/kg	Rapid infusion: IV in normal saline 500 mL over 90 minutes on Days 1 and 15: infuse 100 mL over 30 minutes, then infuse the remaining 400 mL over 60 minutes <i>Use 0.2 or 0.22 micron filter</i> *Alert: Pharmacy to ensure final volume in bag = 500 mL *Nursing Alert: IV tubing is primed with daratumumab
cyclophosphamide	300 mg/m ² ; maximum dose 500 mg	Orally once daily in the morning on Days 1, 8, 15 and 22 Take with or without food. Swallow whole (Self-administered at home)
Cycle 7 and Onwards		
cetirizine	10 mg	Orally 30 minutes prior to daratumumab on Day 1
acetaminophen	975 mg	Orally 30 minutes prior to daratumumab on Day 1
dexamethasone	20 mg	Orally 30 minutes prior to daratumumab on Day 1
daratumumab	16 mg/kg	Rapid infusion: IV in normal saline 500 mL over 90 minutes on Day 1: infuse 100 mL over 30 minutes, then infuse the remaining 400 mL over 60 minutes <i>Use 0.2 or 0.22 micron filter</i> *Alert: Pharmacy to ensure final volume in bag = 500 mL *Nursing Alert: IV tubing is primed with daratumumab
All doses will be automatically rounded that fall within the DSG Approved Dose Bands. See LYMP DSG – Dose Banding document for more information		
cyclophosphamide (PROCYTOX®) available dosage strengths: 25 mg and 50 mg tablets Classification: Cytotoxic, Hazardous		

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

REQUIRED MONITORING

Baseline

- RBC serology (genotyping) mandatory prior to starting daratumumab
- Hepatitis B serology

All Cycles

Day 1

- CBC, serum creatinine, urea, electrolytes, liver enzymes, total bilirubin, albumin and glucose as per Physician Orders
- Serum Protein Electrophoresis (SPEP)/Free Light Chain Ratio (FLCH) (response assessment)

Days 8, 15 and 22

- No blood work required

daratumumab (IV) monitoring

All Doses

- Full vital signs (temperature, heart rate, respiratory rate, blood pressure and O₂ saturation) at baseline and as clinically indicated
- No observation period is required after daratumumab administration. Patient can be discharged from treatment room if stable whether they had a reaction or not

Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
valACYclovir	500 mg	Orally once daily
dexamethasone	4 mg	Orally once daily in the morning the day after daratumumab on Day 3 of first cycle only <i>*Alert: dexamethasone is prescribed to prevent delayed infusion reactions (respiratory)</i>
fluticasone and salmeterol combination	100 mcg – 50 mcg per dose	Prescribed at physician's discretion If patient has a history of asthma or COPD, 1 inhalation twice daily only as needed post daratumumab infusion
Cycles 1 to 6 only		
metoclopramide	10 - 20 mg	Orally every 4 hours as needed for nausea and vomiting

DISCHARGE INSTRUCTIONS

All Cycles

- Patients should be instructed to contact their cancer team immediately if symptoms of hypersensitivity reactions occur after discharge
- Instruct patient to take recommended support medications at home

Cycles 1 to 6

- Instruct patient to take dexamethasone and cyclophosphamide at home in the morning, as they are both part of the cancer therapy in this treatment regimen
- Instruct patient to:
 - Maintain oral intake of 2000 mL (8 glasses) of fluid daily at home
 - Empty bladder every 2 hours while awake and at bedtime for 24 hours after each dose of cyclophosphamide
 - Obtain immediate assistance as per your clinic's contact instructions if:
 - Symptoms of hemorrhagic cystitis (e.g. dysuria, hematuria)
 - Unable to drink recommended amount of fluid
- bortezomib has potential for drug-drug interactions. Patients should notify clinic prior to starting any new medication
- Advise patient to avoid green tea to prevent interactions with bortezomib
- Avoid grapefruit and grapefruit juice, Seville oranges (i.e. orange marmalade), and starfruit
- Reinforce applicable safe handling precautions of medications, blood and body fluids for 48 hours after completion of chemotherapy

ADDITIONAL INFORMATION

- daratumumab interferes with cross-matching and red blood cell antibody screening. **Indicate on all Canadian Blood Services requisitions that the patient is on daratumumab**
- daratumumab may interfere with the interpretation of the Serum Protein Electrophoresis (SPEP) results. **Indicate on all immunology (SPEP) requisitions that the patient is on daratumumab**
- Administering nurse must document any infusion-related reactions with any dose of daratumumab
- valACYclovir (shingles prophylaxis) continues while on treatment and for 1 month after discontinuation of treatment due to risk of prolonged immunosuppression
- All patients should be considered for bisphosphonate therapy
- Administration site restrictions are in place for daratumumab. Cycle 1, Days 1 and 2 must be administered at CCMB MacCharles in Winnipeg
- **Note: At Cycles 2 and 7**, an entry called “**Physician Reminder – dexamethasone dose evaluation**” will appear in the electronic drug order. **No action is required. This prompt is to remind the prescriber to evaluate the dexamethasone dose that begins at Cycles 2 and 7**