Regimen Reference Order

MYEL – daratumumab + carfilzomib + dexamethasone (DKd) (SUBCUTANEOUS daratumumab injection)

ARIA: MYEL - [DKd (SUBCUT)]

Planned Course: **Until disease progression or unacceptable toxicity (1 cycle = 28 days)**
Indication for Use: **Multiple Myeloma Relapsed/Refractory**

CVAD: At Provider's Discretion

Proceed with treatment if:

carfilzomib:

Day 1 of every cycle & Day 15 of Cycles 1 and 2

- ***ANC equal to or greater than 0.5 x 10^9/L AND Platelets equal to or greater than 30 x 10^9/L***

daratumumab:

- ***On Day 1, proceed with daratumumab only when carfilzomib starts***
- ***On subsequent treatment days, proceed with daratumumab regardless of CBC***
  - ❖ **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 of 6 to 8 cups of liquid per day starting at least 48 hours before Cycle 1 only (unless other directed by clinic i.e. fluid restriction) **(Self-administered at home)**		
allopurinol*	300 mg	Orally once daily for 10 days to begin 3 days prior to Cycle 1 and at provider's discretion for subsequent cycles **(Self-administered at home)** *Only patients at risk of tumor lysis syndrome will be prescribed allopurinol

Treatment Regimen
MYEL – daratumumab + carfilzomib + dexamethasone (DKd) (SUBCUTANEOUS daratumumab injection)

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
Cycle 1		
normal saline	500 mL	IV over 1 hour prior to carfilzomib on **Days 1, 8 and 15** (Pre hydration)
cetirizine	10 mg	Orally at least **1 hour** prior to daratumumab on **Days 1, 8, 15 and 22**

acetaminophen	975 mg	Orally at least **1 hour** prior to daratumumab on **Days 1, 8, 15 and 22**	
montelukast	10 mg	Orally at least **1 hour** prior to daratumumab on **Day 1 ONLY**	
dexamethasone	20 mg	**Day 1**	IV in normal saline 50 mL over 15 minutes at least **1 hour** prior to daratumumab **Nursing Alert: daratumumab starts at least **1 hour after completion** of dexamethasone*
		Days 8 and 15	Orally at least **1 hour** prior to daratumumab and at least 30 minutes prior to carfilzomib
		Day 22	Orally at least **1 hour** prior to daratumumab
If applicable, wait 30 minutes after completion of IV pre-medication(s) before starting carfilzomib			
carfilzomib	20 mg/m^2	IV in D5W 100 mL over 30 minutes on **Day 1**	
	70 mg/m^2	IV in D5W 100 mL over 30 minutes on **Days 8 and 15**	
normal saline	500 mL	IV over the 1-hour observation period on **Days 1, 8 and 15** (Post hydration)	
daratumumab (Subcutaneous)	1800 mg (1800 mg = 15 mL)	**Subcutaneous:** Administer over 3 to 5 minutes into abdomen on **Days 1, 8, 15 and 22** Remove vial from refrigerator 30 minutes prior to preparing dose to bring to ambient temperature (15°C to 30°C) Use 23G needle **Nursing Alert: Ensure subcutaneous daratumumab formulation is used (daratumumab-hyaluronidase)* **Nursing Alert: A 3-hour observation period is required after first dose (Day 1 only) if patient has never previously received daratumumab*	
dexamethasone	20 mg	Orally once daily in the morning with food on **Days 2, 9, 16 and 23 (Self-administered at home)**	
Cycle 2			
dexamethasone	40 mg	Orally once daily in the morning with food on **Days 1, 8, 15 and 22 (Self-administered at home)** **Alert: On days of carfilzomib administration, dexamethasone should be taken between 30 minutes to 4 hours prior to carfilzomib*	
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**	
carfilzomib	70 mg/m^2	IV in D5W 100 mL over 30 minutes on **Days 1, 8 and 15**	
daratumumab (Subcutaneous)	1800 mg (1800 mg = 15 mL)	**Subcutaneous:** Administer over 3 to 5 minutes into abdomen on **Days 1, 8, 15 and 22** Remove vial from refrigerator 30 minutes prior to preparing dose to bring to ambient temperature (15°C to 30°C) Use 23G needle **Nursing Alert: Ensure subcutaneous daratumumab formulation is used (daratumumab-hyaluronidase)*	

Cycles 3 to 6		
dexamethasone	40 mg	Orally once daily in the morning with food on **Days 1, 8, 15 and 22** **(Self-administered at home)** **Alert: On days of carfilzomib administration, dexamethasone should be taken between 30 minutes to 4 hours prior to carfilzomib*
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**
carfilzomib	70 mg/m^2	IV in D5W 100 mL over 30 minutes on **Days 1, 8 and 15**
daratumumab (Subcutaneous)	1800 mg (1800 mg = 15 mL)	**Subcutaneous:** Administer over 3 to 5 minutes into abdomen on **Days 1 and 15** Remove vial from refrigerator 30 minutes prior to preparing dose to bring to ambient temperature (15°C to 30°C) Use 23G needle **Nursing Alert: Ensure subcutaneous daratumumab formulation is used (daratumumab-hyaluronidase)*
Cycle 7 and Onwards		
dexamethasone	40 mg	Orally once daily in the morning with food on **Days 1, 8, 15 and 22** **(Self-administered at home)** **Alert: On days of carfilzomib administration, dexamethasone should be taken between 30 minutes to 4 hours prior to carfilzomib*
cetirizine	10 mg	Orally 30 minutes prior to daratumumab on **Day 1**
acetaminophen	975 mg	Orally 30 minutes prior to daratumumab on **Day 1**
carfilzomib	70 mg/m^2	IV in D5W 100 mL over 30 minutes on **Days 1, 8 and 15**
daratumumab (Subcutaneous)	1800 mg (1800 mg = 15 mL)	**Subcutaneous:** Administer over 3 to 5 minutes into abdomen on **Day 1** Remove vial from refrigerator 30 minutes prior to preparing dose to bring to ambient temperature (15°C to 30°C) Use 23G needle **Nursing Alert: Ensure subcutaneous daratumumab formulation is used (daratumumab-hyaluronidase)*
All doses will be automatically rounded that fall within CCMB Approved Dose Bands. See Dose Banding document for more information		

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

Cycles 1 and 2 (also see carfilzomib and daratumumab monitoring below)

Day 1

- CBC, serum creatinine, urea, electrolytes, liver enzymes, total bilirubin, albumin and glucose as per Physician Orders
- Physician should assess patient for signs and symptoms of cardiotoxicity prior to each cycle
- Serum Protein Electrophoresis (SPEP)/Free Light Chain Ratio (FLCH) (response assessment)

Day 15

- CBC, serum creatinine, urea, electrolytes, liver enzymes, total bilirubin, albumin, glucose and reticulocyte as per Physician Orders

Days 8 and 22

- No blood work required

Cycle 3 and Onwards

Day 1

- CBC, serum creatinine, urea, electrolytes, liver enzymes, total bilirubin, albumin and glucose as per Physician Orders
- Physician should assess patient for signs and symptoms of cardiotoxicity prior to each cycle
- SPEP/FLCH (response assessment)

carfilzomib monitoring

- Patient should be assessed for signs and symptoms of fluid overload prior to each carfilzomib dose
- Full vital signs (temperature, heart rate, respiratory rate, blood pressure and O_2 saturation) at baseline and as clinically indicated
- Observe patient for 1 hour after carfilzomib infusion for Cycle 1 only (during Post hydration). Full vital signs after observation period is complete

daratumumab (subcutaneous injection) monitoring

Cycle 1, Day 1

- Full vital signs (temperature, heart rate, respiratory rate, blood pressure and O_2 saturation) at baseline and as clinically indicated
- Observe patient for **3 hours** after subcutaneous daratumumab administration if patient has never previously received daratumumab. Full vital signs prior to discharge

Cycle 1, Day 8 and Onwards

- Full vital signs (temperature, heart rate, respiratory rate, blood pressure and O_2 saturation) at baseline and as clinically indicated
- No observation period is required after subcutaneous daratumumab administration if patient tolerated previous doses of subcutaneous daratumumab

Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
valACYclovir	500 mg	Orally once daily
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 injection

DISCHARGE INSTRUCTIONS

- Patients should be instructed to contact their cancer team immediately if symptoms of hypersensitivity reactions occur after discharge
- dexamethasone is a cancer therapy in this treatment regimen. Remind patient to take dexamethasone at home.
- Remind patients to take recommended support medications at home
- Reinforce oral hydration of 6 to 8 cups of liquid per day
- Patients should be instructed to inform their cancer team of shortness of breath or signs and symptoms of fluid overload
- Reinforce applicable safe handling precautions of medications, blood and body fluids for 48 hours after completion of carfilzomib

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
- carfilzomib has been associated with cardiotoxicity
- Consideration may be given to reducing dexamethasone dose at the physician's discretion to 20 mg for patients older than 75 years or have a body-mass index of less than 18.5 kg/m^2
- 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
- **Note: At Cycle 2**, 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 Cycle 2**