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**

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 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		
dexamethasone	40 mg	Orally once daily in the morning with food on **Days 1, 8, 15 and 22** **(Self-administered at home)**

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**
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)*
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*
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*
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*
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

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

Baseline
- RBC serology (genotyping) mandatory prior to starting daratumumab

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 monitoring

- 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. 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
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
- 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) 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**