

## Regimen Reference Order – MYEL – DVd (IV daratumumab)

ARIA: MYEL - [DVd (IV)]

Planned Course: Until disease progression or unacceptable toxicity (1 cycle = 28 days)

Indication for Use: Relapsed/Refractory Multiple Myeloma

CVAD: At Provider's Discretion

### Proceed with treatment if:

#### Day 1

ANC equal to or greater than  $1 \times 10^9/L$  AND Platelets equal to or greater than  $30 \times 10^9/L$

❖ Contact Hematologist if parameters not met

## SEQUENCE OF MEDICATION ADMINISTRATION

### Pre-treatment Requirements

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

### Treatment Regimen – MYEL – DVd (IV daratumumab)

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
<b>Cycle 1</b>		
cetirizine	10 mg	Orally <b>1 hour</b> prior to daratumumab on <b>Days 1, 2, 8, 15 and 22</b>
acetaminophen	975 mg	Orally <b>1 hour</b> prior to daratumumab on <b>Days 1, 2, 8, 15 and 22</b>
dexamethasone	20 mg	IV in normal saline 50 mL over 15 minutes <b>1 hour</b> prior to daratumumab on <b>Days 1, 2, 8, 15 and 22</b> <i>*Nursing Alert: daratumumab starts 1 hour after completion of dexamethasone</i>
bortezomib	1.5 mg/m <sup>2</sup>	Subcutaneous injection once weekly on <b>Days 1, 8, 15 and 22</b>

Wait 1 hour after completion of IV pre-medication(s) before starting daratumumab

daratumumab	8 mg/kg	<p><b>Slow infusion:</b> IV in normal saline 500 mL on <b>Days 1 and 2</b> following administration rates below:</p> <ul style="list-style-type: none"> <li>• 0 to 60 minutes – 50 mL/hour</li> <li>• 60 to 120 minutes – 100 mL/hour</li> <li>• 120 to 180 minutes – 150 mL/hour</li> <li>• 180 minutes onwards – 200 mL/hour</li> </ul> <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><b>Rapid infusion:</b> IV in normal saline 500 mL over 90 minutes on <b>Days 8, 15, and 22:</b> 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>
dexamethasone	20 mg	Orally once daily in the morning with food on <b>Days 9, 16 and 23 (Self-administered at home)</b>
<b>Cycle 2</b>		
dexamethasone	40 mg	Orally once daily in the morning with food on <b>Days 1, 8, 15 and 22 (Self-administered at home)</b>
cetirizine	10 mg	Orally 30 minutes prior to daratumumab on <b>Days 1, 8, 15 and 22</b>
acetaminophen	975 mg	Orally 30 minutes prior to daratumumab on <b>Days 1, 8, 15 and 22</b>
bortezomib	1.5 mg/m <sup>2</sup>	Subcutaneous injection once weekly on <b>Days 1, 8, 15 and 22</b>
daratumumab	16 mg/kg	<p><b>Rapid infusion:</b> IV in normal saline 500 mL over 90 minutes on <b>Days 1, 8, 15 and 22:</b> 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>
<b>Cycles 3 and 4</b>		
dexamethasone	40 mg	Orally once daily in the morning with food on <b>Days 1, 8, 15 and 22 (Self-administered at home)</b>
cetirizine	10 mg	Orally 30 minutes prior to daratumumab on <b>Days 1 and 15</b>
acetaminophen	975 mg	Orally 30 minutes prior to daratumumab on <b>Days 1 and 15</b>
bortezomib	1.5 mg/m <sup>2</sup>	Subcutaneous injection once weekly on <b>Days 1, 8, 15 and 22</b>
daratumumab	16 mg/kg	<p><b>Rapid infusion:</b> IV in normal saline 500 mL over 90 minutes on <b>Days 1 and 15:</b> 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>

Cycles 5 to 8		
dexamethasone	40 mg	Orally once daily in the morning with food on <b>Days 1, 8, 15 and 22</b> <b>(Self-administered at home)</b>
cetirizine	10 mg	Orally 30 minutes prior to daratumumab on <b>Day 1</b>
acetaminophen	975 mg	Orally 30 minutes prior to daratumumab on <b>Day 1</b>
bortezomib	1.5 mg/m <sup>2</sup>	Subcutaneous injection once weekly on <b>Days 1, 8, 15 and 22</b>
daratumumab	16 mg/kg	<b>Rapid infusion:</b> IV in normal saline 500 mL over 90 minutes on <b>Day 1:</b> infuse 100 mL over 30 minutes, then infuse the remaining 400 mL over 60 minutes Use 0.2 or 0.22 micron filter <i>*Alert: Pharmacy to ensure final volume in bag = 500 mL</i> <i>*Nursing Alert: IV tubing is primed with daratumumab</i>
Cycle 9* and Onwards		
cetirizine	10 mg	Orally 30 minutes prior to daratumumab on <b>Day 1</b>
acetaminophen	975 mg	Orally 30 minutes prior to daratumumab on <b>Day 1</b>
dexamethasone	20 mg	Orally 30 minutes prior to daratumumab on <b>Day 1</b>
daratumumab	16 mg/kg	<b>Rapid infusion:</b> IV in normal saline 500 mL over 90 minutes on <b>Day 1:</b> infuse 100 mL over 30 minutes, then infuse the remaining 400 mL over 60 minutes Use 0.2 or 0.22 micron filter <i>*Alert: Pharmacy to ensure final volume in bag = 500 mL</i> <i>*Nursing Alert: IV tubing is primed with daratumumab</i>
<p><b>*At physician's discretion, bortezomib may be prescribed Cycle 9 and onwards as maintenance on Days 1 and 15</b></p> <p>All doses will be automatically rounded that fall within the DSG Approved Dose Bands. See LYMP DSG – Dose Banding Document for more information</p>		

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 to 8

#### 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

### Cycle 9 and Onwards

#### Day 1

- CBC, serum creatinine, urea, electrolytes, liver enzymes, total bilirubin, albumin and glucose as per Physician Orders
- SPEP/FLCH (response assessment)

## daratumumab monitoring

## All Doses

- Full vital signs (temperature, heart rate, respiratory rate, blood pressure and O<sub>2</sub> 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 in the morning the day after daratumumab on <b>Day 3</b> of Cycle 1 only <i>Note: 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

## DISCHARGE INSTRUCTIONS

## All Cycles

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

## Cycles 1 to 8

- dexamethasone is a cancer therapy in this treatment regimen. Remind patient to take dexamethasone at home
- 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
- Consideration may be given to reducing dexamethasone dose at the physician's discretion to 20 mg for patients older than 75 years or who have a body mass index of less than 18.5 kg/m<sup>2</sup>
- 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 9**, 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 9**