

Regimen Reference Order – MYEL – daratumumab + bortezomib + dexamethasone (DVd) ARIA: MYEL - [DVd]

Planned Course: Every 28 days until disease progression or unacceptable toxicity

Indication for Use: Relapsed Multiple Myeloma

CVAD: At Provider's Discretion

Proceed with treatment if:

Day 1 of every cycle

bortezomib:

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

daratumumab:

- **On Day 1, proceed with daratumumab only when bortezomib starts**
- **On subsequent treatment days, proceed with daratumumab regardless of CBC**

Day 15 of Cycles 1 and 2 only

bortezomib:

- **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 for 5 days, starting the day before each daratumumab dose of Cycle 1 Cycle 2 onwards at the discretion of the physician <i>*Nursing Alert: Notify physician if patient has not taken montelukast (Self-administered at home)</i>

Treatment Regimen – MYEL – daratumumab + bortezomib + dexamethasone (DVd)

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
Cycle 1		
acetaminophen	975 mg	Orally 1 hour prior to daratumumab on Days 1, 2, 8, 15 and 22
dexamethasone	20 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>

diphenhydrAMINE	50 mg	IV in normal saline 50 mL over 15 minutes 1 hour prior to daratumumab on Days 1, 2, 8, 15 and 22
daratumumab	8 mg/kg	IV in normal saline 500 mL on Days 1 and 2 following administration rates below: <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 Use 0.2 or 0.22 micron filter <i>*Nursing Alert: IV tubing is primed with daratumumab</i>
	16 mg/kg	IV in normal saline 500 mL on Day 8 following administration rates below: <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 Use 0.2 or 0.22 micron filter <i>*Nursing Alert: IV tubing is primed with daratumumab</i>
	16 mg/kg	IV in normal saline 500 mL on Days 15 and 22 following administration rates below: <ul style="list-style-type: none"> • 0 to 60 minutes – 100 mL/hour • 60 to 120 minutes – 150 mL/hour • 120 minutes onwards - 200 mL/hour Use 0.2 or 0.22 micron filter <i>*Nursing Alert: IV tubing is primed with daratumumab</i>
bortezomib	1.5 mg/m ²	Subcutaneous injection once weekly on Days 1, 8, 15 and 22
dexamethasone	20 mg	Orally once daily in the morning on Days 9, 16 and 23 (Self-administered at home)
Cycle 2		
acetaminophen	975 mg	Orally 1 hour prior to daratumumab on Days 1, 8, 15 and 22
dexamethasone	20 mg	IV in normal saline 50 mL over 15 minutes 1 hour prior to daratumumab on Days 1, 8, 15 and 22 <i>*Nursing Alert: daratumumab starts 1 hour after completion of dexamethasone</i>
diphenhydrAMINE	50 mg	IV in normal saline 50 mL over 15 minutes 1 hour prior to daratumumab 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, 8, 15, and 22: infuse 100 mL over 30 minutes, then infuse the remaining 400 mL over 60 minutes Use 0.2 or 0.22 micron filter <i>*Nursing Alert: IV tubing is primed with daratumumab</i>
bortezomib	1.5 mg/m ²	Subcutaneous injection once weekly on Days 1, 8, 15 and 22
dexamethasone	20 mg	Orally once daily in the morning on Days 2, 9, 16 and 23 (Self-administered at home)

Cycles 3 and 4		
acetaminophen	975 mg	Orally 1 hour prior to daratumumab on Days 1 and 15
dexamethasone	20 mg	IV in normal saline 50 mL over 15 minutes 1 hour prior to daratumumab on Days 1 and 15 <i>*Nursing Alert: daratumumab starts 1 hour after completion of dexamethasone</i>
diphenhydrAMINE	50 mg	IV in normal saline 50 mL over 15 minutes 1 hour prior to daratumumab on Days 1 and 15
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 Use 0.2 or 0.22 micron filter <i>*Nursing Alert: IV tubing is primed with daratumumab</i>
bortezomib	1.5 mg/m ²	Subcutaneous injection once weekly on Days 1, 8, 15 and 22
dexamethasone	20 mg	Orally once daily in the morning on Days 2 and 16 (Self-administered at home)
dexamethasone	40 mg	Orally once daily in the morning on Days 8 and 22 (Self-administered at home)
Cycles 5 to 8		
acetaminophen	975 mg	Orally 1 hour prior to daratumumab on Day 1
dexamethasone	20 mg	IV in normal saline 50 mL over 15 minutes 1 hour prior to daratumumab on Day 1 <i>*Nursing Alert: daratumumab starts 1 hour after completion of dexamethasone</i>
diphenhydrAMINE	50 mg	IV in normal saline 50 mL over 15 minutes 1 hour 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 Use 0.2 or 0.22 micron filter <i>*Nursing Alert: IV tubing is primed with daratumumab</i>
bortezomib	1.5 mg/m ²	Subcutaneous injection once weekly on Days 1, 8, 15 and 22
dexamethasone	20 mg	Orally once daily in the morning on Day 2 (Self-administered at home)
dexamethasone	40 mg	Orally once daily in the morning on Days 8, 15 and 22 (Self-administered at home)
Cycle 9* and onwards		
acetaminophen	975 mg	Orally 1 hour prior to daratumumab
dexamethasone	20 mg	IV in normal saline 50 mL over 15 minutes 1 hour prior to daratumumab <i>*Nursing Alert: daratumumab starts 1 hour after completion of dexamethasone</i>

diphenhydrAMINE	50 mg	IV in normal saline 50 mL over 15 minutes 1 hour prior to daratumumab
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 Use 0.2 or 0.22 micron filter <i>*Nursing Alert: IV tubing is primed with daratumumab</i>
dexamethasone	20 mg	Orally once daily in the morning on Day 2 (Self-administered at home)
<p>* At physician's discretion, bortezomib may be prescribed Cycles 9 and onwards as maintenance on Days 1 and 15</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>		

Flush after each medication:

- 50 mL over 6 minutes (500 mL/hr)

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

Cycles 1 and 2

Day 1

- CBC, biochemistry, as per Physician Orders
- SPEP/FLCI (response assessment)

Day 15

- CBC

Days 8 and 22

- No blood work required

Cycles 3 to 6

Day 1

- CBC, biochemistry as per physician order
- SPEP/FLCI (response assessment)

Days 8, 15 and 22

- No blood work required

Cycle 7 and onwards

Day 1

- CBC, biochemistry as per Physician Orders
- SPEP/FLCI (response assessment)

daratumumab monitoring**Cycle 1, Days 1 and 2**

- Full vital signs (temperature, heart rate, respiratory rate, blood pressure and O₂ saturation)
 - at baseline, then
 - blood pressure and heart rate every 15 minutes for 1 hour, then
 - blood pressure and heart rate every 30 minutes for 1 hour, then
 - blood pressure and heart rate every hour until infusion complete

Subsequent Doses

- Full vital signs at baseline and then as clinically indicated

Observation periods

- No observation periods. Patient can be discharged from treatment room if stable whether they had a reaction or not

Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
valACYlovir	500 mg	Orally once daily
predniSONE	25 mg	Orally once daily in the morning the day after daratumumab on Day 3 of first cycle only <i>Alert: predniSONE is prescribed to prevent delayed infusion reactions (respiratory)</i>
salmeterol and fluticasone combination (Advair® Diskus)	100 mcg - 50 mcg per dose Diskus inhaler	Prescribed at physician's discretion If patient has a history of asthma or COPD, inhale 1 puff twice daily only as needed post infusion

DISCHARGE INSTRUCTIONS

- Remind patient to take predniSONE and dexamethasone at home
- Advise patient to avoid green tea to prevent interactions with bortezomib
- 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 have a body-mass index of less than 18.5 kg/m²
- All patients should be considered for bisphosphonate therapy
- Administration site restrictions are in place for daratumumab. Cycle 1, Days 1, 2, and 8 must be administered at CCMB MacCharles in Winnipeg