

Regimen Reference Order – MYEL – daratumumab + lenalidomide + dexamethasone (DRd)

ARIA: MYEL - [DRd]

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:

Day 1 of every cycle

lenalidomide:

- 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 lenalidomide starts
- On subsequent treatment days, proceed with daratumumab regardless of blood counts

Day 15 of Cycles 1 and 2 only

lenalidomide:

- 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</i> (Self-administered at home)

Treatment Regimen – MYEL – daratumumab + lenalidomide + dexamethasone (DRd)		
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

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 <i>*Nursing Alert: daratumumab starts 1 hour after completion of IV pre-medications</i>
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>
lenalidomide	25 mg	Orally once daily on Days 1 to 21, then 7 days off . Can be taken any time of day (Self-administered at home)
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 over 15 minutes 1 hour prior to daratumumab on Days 1, 8, 15 and 22
diphenhydrAMINE	50 mg	IV in normal saline 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 IV pre-medications</i>

daratumumab	16 mg/kg	IV in normal saline 500 mL on Days 1, 8, 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>
lenalidomide	25 mg	Orally once daily on Days 1 to 21, then 7 days off . Can be taken any time of day (Self-administered at home)
dexamethasone	20 mg	Orally once daily in the morning on Days 2, 9, 16 and 23 (Self-administered at home)
Cycles 3 to 6		
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
diphenhydrAMINE	50 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 IV pre-medications</i>
daratumumab	16 mg/kg	IV in normal saline 500 mL on Days 1 and 15 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>
dexamethasone	20 mg	Orally once daily in the morning on Days 2 and 16 (Self-administered at home)
lenalidomide	25 mg	Orally once daily on Days 1 to 21, then 7 days off . Can be taken any time of day (Self-administered at home)
dexamethasone	40 mg	Orally once daily in the morning on Days 8 and 22 (Self-administered at home)
Cycle 7 and onwards		
acetaminophen	975 mg	Orally 1 hour prior to daratumumab on Day 1
dexamethasone	20 mg	IV in normal saline 50 mL 1 hour prior to daratumumab on Day 1
diphenhydrAMINE	50 mg	IV in normal saline 50 mL 1 hour prior to daratumumab on Day 1 <i>*Nursing Alert: daratumumab starts 1 hour after completion of IV pre-medications</i>

daratumumab	16 mg/kg	IV in normal saline 500 mL on Day 1 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>
lenalidomide	25 mg	Orally once daily on Days 1 to 21, then 7 days off . Can be taken any time of day (Self-administered at home)
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)

lenalidomide (Revlimid®) available dosage strengths: 2.5 mg, 5 mg, 10 mg, 15 mg, 20 mg and 25 mg capsules
Classification: Cytotoxic, Hazardous

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 Orders
- 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)

Throughout therapy

- TSH every 3 months as per Physician Orders

daratumumab monitoring

Cycle 1, Days 1 and 2

- Full vital signs (temperature, heart rate, respiration, blood pressure and O₂ saturation)
 - at baseline, then
 - blood pressure and pulse every 15 minutes for 1 hour, then
 - blood pressure and pulse every 30 minutes for 1 hour, then
 - blood pressure and pulse 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
valACYclovir	500 mg	Orally once daily
acetylsalicylic acid (ASA) enteric coated	81 mg delayed release	Orally one 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 lenalidomide and dexamethasone at home
- Reinforce applicable safe handling precautions of medications, blood and body fluids for 48 hours after completion of lenalidomide

ADDITIONAL INFORMATION

- 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
- daratumumab interferes with cross-matching and red blood cell antibody screening. If a transfusion is required, draw Type and Screen and indicate on requisition that the patient is on daratumumab. The nurse must indicate each time, in case it was missed previously
- All patients should be considered for bisphosphonate therapy
- lenalidomide is teratogenic
- Female patients of childbearing potential will require monthly pregnancy tests (βHCG) that must be done within 7 days of the next prescription fill
- Administering nurse must document any infusion-related reactions with any dose of daratumumab
- lenalidomide is controlled by a distribution program requiring prescriptions to be written by a RevAid registered physician and dispensed by a RevAid registered pharmacy
- Administration site restrictions are in place for daratumumab. Cycle 1 must be administered at CCMB MacCharles in Winnipeg. Cycle 2 onwards should only be administered at a site in which a pharmacy is on site