Regimen Reference Order

MYEL – isatuximab + carfilzomib + dexamethasone

ARIA: MYEL - [isatuximab + Kd]

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***

isatuximab:

- ***On Day 1, proceed with isatuximab only when carfilzomib starts***
- ***On subsequent treatment days, proceed with isatuximab 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 otherwise 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 – isatuximab + carfilzomib + dexamethasone

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
Cycle 1		
montelukast	10 mg	Orally **1 hour** prior to isatuximab on Day **1 ONLY**
acetaminophen	975 mg	Orally **1 hour** prior to isatuximab on **Days 1, 8, 15 and 22**
famotidine	40 mg	Orally **1 hour** prior to isatuximab on **Days 1, 8, 15 and 22**
cetirizine	20 mg	Orally **1 hour** prior to isatuximab on **Days 1, 8, 15 and 22**

dexamethasone	40 mg	IV in normal saline 50 mL over 15 minutes **1 hour** prior to isatuximab on **Days 1, 8, 15 and 22** **Nursing Alert: isatuximab starts **1 hour after completion** of dexamethasone infusion*
normal saline	250 mL	IV over 30 minutes on **Days 1, 8 and 15** (Pre hydration for carfilzomib)
Wait 1 hour after completion of IV pre-medication(s) before starting isatuximab		
isatuximab	10 mg/kg	IV in normal saline 250 mL on **Day 1** following administration rates below: • 0 to 60 minutes – 25 mL/hour • 60 to 90 minutes – 50 mL/hour • 90 to 120 minutes – 75 mL/hour • 120 to 150 minutes – 100 mL/hour • 150 to 180 minutes – 125 mL/hour • 180 minutes onwards – 150 mL/hour *Use 0.2 or 0.22 micron filter* **Alert: Pharmacy to ensure final volume in bag = 250 mL* **Nursing Alert: IV tubing is primed with isatuximab*
	10 mg/kg	IV in normal saline 250 mL on **Day 8** following administration rates below: • 0 to 30 minutes – 50 mL/hour • 30 to 60 minutes – 100 mL/hour • 60 minutes onwards – 200 mL/hour *Use 0.2 or 0.22 micron filter* **Alert: Pharmacy to ensure final volume in bag = 250 mL* **Nursing Alert: IV tubing is primed with isatuximab*
	10 mg/kg	IV in normal saline 250 mL over 75 minutes on **Days 15 and 22** *Use 0.2 or 0.22 micron filter* **Alert: Pharmacy to ensure final volume in bag = 250 mL* **Nursing Alert: IV tubing is primed with isatuximab*
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	Infused over the 1-hour observation period on **Days 1, 8 and 15** (Post hydration)
Cycle 2 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: this dexamethasone dose should be taken prior to isatuximab (for Days 1 and 15) and between 30 minutes to 4 hours prior to carfilzomib (for Days 1, 8 and 15)*
acetaminophen	975 mg	Orally **1 hour** prior to isatuximab on **Days 1 and 15**
famotidine	40 mg	Orally **1 hour** prior to isatuximab on **Days 1 and 15**

cetirizine	10 mg	Orally **1 hour** prior to isatuximab on **Days 1 and 15**
isatuximab	10 mg/kg	IV in normal saline 250 mL over 75 minutes on **Days 1 and 15** *Use 0.2 or 0.22 micron filter* **Alert:* *Pharmacy to ensure final volume in bag = 250 mL* **Nursing Alert:* *IV tubing is primed with isatuximab*
carfilzomib	70 mg/m^2	IV in D5W 100 mL over 30 minutes on **Days 1, 8 and 15**
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 isatuximab
- Hepatitis B serology

Cycle 1 (also see isatuximab and carfilzomib monitoring below)
Day 1
- CBC, serum creatinine, urea, electrolytes, liver enzymes, total bilirubin, albumin and glucose as per Physician Orders
- TSH prior to Cycle 1 then every 3 cycles thereafter 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 and glucose as per Physician Orders

Days 8 and 22
- No blood work required

Cycle 2 (also see isatuximab and carfilzomib 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
- SPEP/FLCH (response assessment)

Day 8
- No blood work required

Day 15
- CBC, serum creatinine, urea, electrolytes, liver enzymes, total bilirubin, albumin and glucose as per Physician Orders

Cycle 3 and Onwards (also see isatuximab and carfilzomib monitoring below)
Day 1
- CBC, serum creatinine, urea, electrolytes, liver enzymes, total bilirubin, albumin and glucose as per Physician Orders
- TSH every 3 cycles as per Physician Orders
- Physician should assess patient for signs and symptoms of cardiotoxicity prior to each cycle
- SPEP/FLCH (response assessment)

Days 8 and 15
- No blood work required

isatuximab 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 isatuximab administration. Patient can be discharged from treatment room if stable whether they had a reaction or not

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

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 isatuximab infusion

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
- Instruct patient 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

ADDITIIONAL INFORMATION

- isatuximab interferes with cross-matching and red blood cell antibody screening. **Indicate on all Canadian Blood Services requisitions that the patient is on isatuximab**
- isatuximab may interfere with the interpretation of the Serum Protein Electrophoresis (SPEP) results. **Indicate on all immunology (SPEP) requisitions that the patient is on isatuximab**
- Administering nurse must document any infusion-related reactions with any dose of isatuximab
- carfilzomib has been associated with cardiotoxicity including venous thrombosis, pulmonary toxicity, hepatotoxicity, hematologic toxicities including thrombotic microangiopathy and hemorrhage and posterior reversible encephalopathy syndrome (PRES)
- valACYclovir (shingles prophylaxis) continues during and for 4 weeks after completion of carfilzomib due to immunosuppression
- All patients should be considered for bisphosphonate therapy