Indication	Multiple Myeloma
Treatment Intent	Disease Modification
Frequency and number of cycles	Repeat every 35 days Maximum 12 cycles
Monitoring Parameters pre-treatment	• **Virology screen: Hepatitis B & C, HIV (Hepatitis B includes HBVsAg and HBVcAb).** • FBC baseline and before each dose of Bortezomib. Treat when neutrophils >/= 1.0 x 10^9/L and platelets >/=70 x 10^9/L precycle & if neutrophils >/= 0.75 x 10^9/L or platelets >/= 30 x 10^9/L on a bortezomib dosing day. • U&Es and LFTs before each cycle. • Consider blood glucose monitoring in patients with diabetes and those with signs of glucose intolerance. • Use bortezomib with caution in patients with pre-existing heart disease or with high risk factors. • Patients should be advised to report any new or worsening respiratory symptoms. • **Hepatic Impairment:** o Bortezomib: In moderate or severe hepatic impairment (>1.5 ULN Bilirubin & any AST) reduce to 0.7 mg/m^2 in the first treatment cycle. Consider dose escalation to 1.0 mg/m^2 or further dose reduction to 0.5 mg/m^2 in subsequent cycles based on tolerability. • **Renal Impairment:** o Melphalan: CrCl 30-50ml/min give 50%; CrCl < 30ml/min – clinical decision. o Bortezomib: should be used with caution in patients with CrCl < 20ml/min not undergoing dialysis; however, no specific dosing recommendations have been made. Since dialysis may reduce bortezomib concentrations, bortezomib should be administered after the dialysis procedure. • **Dose modification:** o **Bortezomib** - If Hb < 65g/l transfuse patient and restart treatment when Hb >65g/l. Bortezomib should be withheld for any grade 3 non-haematological (see below for guidance on managing neuropathic toxicities) or Grade 4 haematological toxicities (neutrophils < 0.5 x 10^9/L or platelets < 25 x 10^9/L); once toxicity has settled reinitiate at 75%, (ie 1.3mg/m^2 → 1.0mg/m^2 → 0.7mg/m^2). For Neuropathic Pain and or Peripheral Sensory or Motor Neuropathy dose reductions see table 1. o **Melphalan** - If neutrophils <0.5 x 10^9/L or platelets <25 x 10^9/L during cycle then consider a dose reduction of Melphalan to 75%. o **Prednisolone** - Dose of prednisolone may be reduced in the very elderly or if significant toxicity occurs. • **Common drug interactions: (for comprehensive list refer to BNF/SPC)** The concomitant use of bortezomib with strong CYP3A4 inducers (e.g., rifampicin, carbamazepine, phenytoin, phenobarbital and St. John's Wort) is not recommended, as efficacy may be reduced. CYP3A4 inhibitors (e.g. ketoconazole, ritonavir) should be used with caution and patients monitored for toxicity. • At least 72 hours must elapse between consecutive bortezomib doses. • Consider PCP prophylaxis/ antiviral/ antifungal therapy if lymphocyte count <1.0 x 10^9/L • Bortezomib can affect the ability to drive and use machines. If patients experience fatigue/dizziness or blurred vision they should not drive.
References	SPC accessed online 16.03.2022 KMCC proforma HAEM-MYEL-032 V1

NB For funding information, refer to CDF and NICE Drugs Funding List

Protocol No	HAEM-MYEL-032	Kent and Medway SACT Protocol Disclaimer: No responsibility will be accepted for the accuracy of this information when used elsewhere.	
Version	V2	Written by	M.Archer
Supersedes version	V1	Checked by	H.Paddock O.Okuwa
Date	15.09.2022	Authorising consultant (usually NOG Chair)	H.Mendis

Table 1: Dose modification of bortezomib for neuropathic toxicities

Severity of Peripheral Neuropathy Signs and Symptoms*	**Modification of Dose and Regimen**
Grade 1 (asymptomatic; loss of deep tendon reflexes or paraesthesia) without pain or loss of function	No Action
Grade 1 with pain or Grade 2 (moderate symptoms; limiting instrumental Activities of Daily Living (ADL)**)	Reduce bortezomib to 1 mg/m^2
Grade 2 with pain or Grade 3 (severe symptoms; limiting self-care ADL ***)	Withhold bortezomib therapy until toxicity resolves. When toxicity resolves, reinitiate with a reduced dose of bortezomib at 0.7 mg/m^2 once per week
Grade 4 (life-threatening consequences; urgent intervention indicated)	Discontinue bortezomib
*Grading based on NCI Common Terminology Criteria for Adverse Events (CTCAE) v4.0 **Instrumental ADL: refers to preparing meals, shopping for groceries or clothes, using telephone, managing money etc; ***Self care ADL: refers to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden.	

Repeat every 35 days

Day	Drug	Dose	Route	Infusion Duration	Administration
Day 1, 8, 15 and 22	**BORTEZOMIB**	**1.3mg/m^2**	SC	bolus	
TTO	Drug	Dose	Route	Directions	
Day 1	**MELPHALAN**	**7mg/m^2**	PO	OD days 1 – 4 Store in a refrigerator.	
	PREDNISOLONE	**60mg/m^2**	PO	OM days 1 – 4. Take with or after food	
	Allopurinol	300mg	PO	OD for 7 days on cycle 1 only.	
	Aciclovir	400mg	PO	BD	
	Omeprazole	20mg	PO	OD Day 1-6 whilst on Prednisolone.	