Indication	For the treatment of multiple myeloma: In transplant ineligible patients who have had only 1 prior line of systemic therapy, which contained both an anti-CD38 targeted antibody and lenalidomide and whose disease progressed whilst receiving treatment or after it was received and In transplant ineligible patients who have had only 2 prior lines of systemic therapy and who are refractory to lenalidomide. NB not funded for primary amyloidosis.
Treatment Intent	Disease Modification
Frequency and number of cycles	Repeat every 35 days Continue until disease progression, unacceptable toxicity or patient's choice to stop treatment. A formal medical review as to whether treatment with selinexor in combination with bortezomib and dexamethasone continues or not will be scheduled to occur at least by the end of the second cycle of treatment.
Monitoring Parameters pre-treatment	• **Virology screening:** All new patients referred for systemic anti-cancer treatment should be screened for hepatitis B and C and the result reviewed prior to the start of treatment. Patients not previously tested who are starting a new line of treatment, should also be screened for hepatitis B and C. Further virology screening will be performed following individual risk assessment and clinician discretion. • FBC baseline and before each dose of bortezomib, proceed with bortezomib if neuts >/=0.5 and PLTS >/=25. • Selinexor: proceed if neuts >1 and PLTS >/=75. • U&Es and LFTs baseline, at week 1 and 3 for the first 2 cycles, then at each cycle throughout treatment and as clinically indicated. Sodium levels should be corrected prior to initiation of treatment. • Baseline chest X-ray. • Baseline body weight, nutritional status and volume check before initiation of treatment, repeated at week 1 and 3 for the first 2 cycles and then throughout treatment. Patients should be advised to maintain adequate fluid and caloric intake during treatment. Intravenous hydration should be considered for patients at risk of dehydration. • **Orthostatic/postural hypotension:** Patients should be advised to seek medical advice if they experience symptoms of dizziness, light-headedness or fainting spells which may be due to bortezomib and can be further exacerbated by dehydration due to recurrent diarrhoea or vomiting from selinexor therapy. • Regular monitoring of blood glucose is recommended for patients on oral antidiabetic agents receiving bortezomib treatment. • **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. o **Selinexor:** No dose adjustment required in mild hepatic impairment. There are insufficient data in patients with moderate or severe hepatic impairment to support a dose recommendation. • **Renal impairment:** 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. ○ **Selinexor:** No dose adjustment required in mild, moderate, or severe renal impairment. There are no data in end-stage renal disease or haemodialysis to support a dose recommendation. • **Management of adverse reactions and dose adjustments:** • Tumour lysis syndrome (TLS): Cases of TLS have been observed in patients treated with selinexor and bortezomib, patients at high risk of TLS should be monitored closely. • **Bortezomib:** ○ Use bortezomib with caution in patients with pre-existing heart disease or with high risk factors. ○ The management of haematological and non-haematological adverse reactions may require dose reduction, interruption or discontinuation of treatment. ○ **Haematological toxicity** ○ If Hb < 65g/l transfuse patient and restart treatment when Hb >65g/l. ○ Bortezomib should be withheld for any 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% e.g. 1.3mg/m^2 to 1mg/m^2, or from 1mg/m^2 to 0.7mg/m^2. ○ **Non-haematological toxicity:** ○ Neuropathic pain and/or peripheral neuropathy: see table 3 ○ For any other >/= Grade 3 non-haematological toxicities considered to be related to bortezomib therapy then this should be withheld until symptoms of the toxicity have resolved to </= Grade 2. Bortezomib may then be reinitiated at a dose reduced by one dose level (from 1.3mg/m^2 to 1mg/m^2, or from 1mg/m^2 to 0.7mg/m^2). ○ Monitor patients for pulmonary symptoms indicative of ILD/pneumonitis and ARDS (e.g. hypoxia, cough, dyspnoea). Patients should be advised to report any new or worsening pulmonary symptoms. ○ **Bortezomib doses reduced for toxicity should not be re-escalated.** • **Selinexor:** ○ The management of haematological and non-haematological adverse reactions may require dose reduction, interruption or discontinuation of treatment. The recommended dose reduction is; first dose reduction 80mg once weekly, second dose reduction, 60mg once weekly. And third dose reduction, 40mg once weekly. If selinexor is not tolerated at 40mg once weekly treatment should be discontinued, (see table A). See table 1 for and table 2 for dose modification for adverse events. ○ For Grade 3 or 4 (life threatening) non-haematologic adverse reactions **not** included in table 2, interrupt selinexor, monitor until resolved to Grade 2 or lower and restart selinexor at 1 dose level lower. • **Common drug interactions (for comprehensive list refer to BNF/SPC):** ○ **Bortezomib:** 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. ○ **Selinexor:** no formal drug interaction studies have been conducted. • **Missed dose:** ○ Selinexor: if a dose is missed or a patient vomits after a dose they should not take another dose and take their next dose at the usual scheduled time. ○ Bortezomib: Omitted doses of bortezomib should not subsequently be made up. At least 72 hours must elapse between consecutive bortezomib doses.

	• **Contraception and pregnancy:** Women of childbearing potential must use effective contraceptive measures and avoid becoming pregnant while being treated with bortezomib and for 8 months following completion of treatment. Male patients should use effective contraceptive measures and be advised not to father a child while receiving bortezomib and for 5 months following completion of treatment. • **Driving and operating machinery:** Bortezomib and Selinexor can affect the ability to drive and use machines. If patients experience fatigue/dizziness or blurred vision or confusion they should not drive. • **For oral self-administration:** refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet and Cancerbackup information sheet.
References	KMCC protocol HAEM-MYEL-049 V2 SPC accessed online 31.12.2025 CDF list V1.381 accessed online 31.12.2025

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

Table A: Selinexor dose modification steps for adverse reactions

	Selinexor in combination with Bortezomib and Dexamethasone (SVd)
Recommended starting dose	100 mg once weekly
First reduction	80 mg once weekly
Second reduction	60 mg once weekly
Third reduction	40 mg once weekly
Discontinue if not tolerated at 40mg	

Table 1 Guidance for Selinexor Haematologic adverse reactions		
Adverse reaction[a]	**Occurrence**	**Action**
Thrombocytopenia		
Platelet count 25,000 to less than 75,000/mcL	Any	• Reduce selinexor by 1 dose level
Platelet count 25,000 to less than 75,000/mcL with concurrent bleeding	Any	• Interrupt selinexor. • Restart selinexor at 1 dose level lower), after bleeding has resolved.
Platelet count less than 25,000/mcL	Any	• Interrupt selinexor. • Monitor until platelet count returns to at least 50,000/mcL. • Restart selinexor at 1 dose level lower.
Neutropenia		
Absolute neutrophil count of 0.5 to 1.0 x 10^9/L without fever	Any	• Reduce selinexor by 1 dose level.
Absolute neutrophil count less than 0.5 x 10^9/L OR Febrile neutropenia	Any	• Interrupt selinexor. • Monitor until neutrophil counts return to 1.0 x 10^9/L or higher. • Restart selinexor at 1 dose level lower.
Anaemia		
Haemoglobin less than 8.0 g/dL	Any	• Reduce selinexor by 1 dose level. • Administer blood transfusions and/or other treatments per clinical guidelines.
Life-threatening consequences (urgent intervention indicated)	Any	• Interrupt selinexor. • Monitor haemoglobin until levels return to 8 g/dL or higher. • Restart selinexor at 1 dose level lower. • Administer blood transfusions and/or other treatments per clinical guidelines.

Table 2 Guidance for selinexor non-haematologic adverse reactions		
Adverse reaction[a]	**Occurrence**	**Action**
Hyponatraemia		
Sodium level 130 mmol/L or less	Any	• Interrupt selinexor and provide appropriate supportive care. • Monitor until sodium levels return to 130 mmol/L or higher. • Restart selinexor at 1 dose level lower.
Fatigue		
Grade 2 lasting greater than 7 days OR Grade 3	Any	• Interrupt selinexor. • Monitor until fatigue resolves to Grade 1 or baseline. • Restart selinexor at 1 dose level lower.
Nausea and vomiting		
Grade 1 or 2 nausea (oral intake decreased without significant weight loss, dehydration or malnutrition) OR Grade 1 or 2 vomiting (5 or fewer episodes per day)	Any	• Maintain selinexor and initiate additional anti-nausea medicinal products.
Grade 3 nausea (inadequate oral caloric or fluid intake) OR Grade 3 or higher vomiting (6 or more episodes per day)	Any	• Interrupt selinexor. • Monitor until nausea or vomiting has resolved to Grade 2 or lower or baseline. • Initiate additional anti-nausea medicinal products. • Restart selinexor at 1 dose level lower.
Diarrhoea		
Grade 2 (increase of 4 to 6 stools per day over baseline)	1st	• Maintain selinexor and institute supportive care.
	2nd and subsequent	• Reduce selinexor by 1 dose level. • Institute supportive care.
Grade 3 or higher (increase of 7 stools or more per day over baseline; hospitalization indicated)	Any	• Interrupt selinexor and institute supportive care. • Monitor until diarrhoea resolves to Grade 2 or lower. • Restart selinexor at 1 dose level lower.
Weight loss and anorexia		
Weight loss of 10% to less than 20% OR Anorexia associated with significant weight loss or malnutrition	Any	• Interrupt selinexor and institute supportive care. • Monitor until weight returns to more than 90% of baseline weight. • Restart selinexor at 1 dose level lower.
Ocular adverse reactions		
Grade 2, excluding cataract	Any	• Perform ophthalmologic evaluation. • Interrupt selinexor and provide supportive care. • Monitor until ocular symptoms resolve to Grade 1 or baseline. • Restart selinexor at 1 dose level lower.
Grade ≥3, excluding cataract	Any	• Permanently discontinue selinexor. • Perform ophthalmologic evaluation.

Table 3 Guidance for bortezomib induced neuropathic pain and/or peripheral neuropathy

NCI CTCAE Grade	**Bortezomib dose**
Grade 1 (asymptomatic; loss of deep tendon reflexes or paraesthesia) with no pain or loss of function	No action
Grade 1 with pain or Grade 2 (moderate symptoms; limiting instrumental activities of daily living such as preparing meals, shopping for groceries or clothes, using telephone, managing money, etc)	Reduce to 1mg/m^2
Grade 2 with pain or Grade 3 (severe symptoms; limiting self-care activities of daily living such as bathing, dressing and undressing, feeding self, using the toilet, taking medicinal products, and not bedridden)	Withhold bortezomib treatment until symptoms of toxicity have resolved. When toxicity resolves, re-initiate bortezomib treatment and reduce dose to 0.7mg/m^2 once per week.
Grade 4 (life threatening consequences; urgent intervention indicated) and/or severe autonomic neuropathy	Discontinue bortezomib

Repeat every 35 days

Day	Drug	Dose	Route	Infusion Duration	Administration
Day 1, 8, 15 and 22	**BORTEZOMIB**	**1.3mg/m²**	SC	bolus	Inject in to the thigh or abdomen at a 45-90° angle. Injection sites should be rotated from left to right.
TTO	Drug	Dose	Route	Directions	
Day 1	**SELINEXOR**	**100mg** **Max dose 70mg/m²**	PO	Take **ONCE** a week on day 1, 8, 15,22 and 29 Swallow whole with water, do not crush, chew or split the tablet. Available as 20mg tablets	
	DEXAMETHASONE	**20mg**	PO	OM on days 1 and 2, 8 and 9, 15 and 16, 22 and 23, 29 and 30. Take with or after food. Take 30minutes before selinexor dose.	
	Ondansetron	8mg	PO	BD for 3 days on day 1, 8, 15, 22 and 29	
	Metoclopramide	10mg	PO	Up to TDS PRN Do not take for more than 5 days continuously.	
	Olanzapine *	2.5-5mg	PO	ON for 3 nights after each selinexor dose Dispense on cycle 1 and 2 then only if specified.	
	Omeprazole	20mg	PO	OM	
	Loperamide	2-4mg	PO	Take 4mg (2 capsules) initially, then 2mg (1 capsule) after each loose stool when required. Maximum 16mg (8 capsules) a day. Dispense 30 capsules on cycle 1 then only if specified.	
	Aciclovir	400mg	PO	BD (plus 3 more months after completion of last treatment dose)	
	Co-trimoxazole	480mg	PO	TWICE daily on Mondays, Wednesdays and Fridays (plus 3 more months after completion of last treatment dose)	
	Fluconazole	50mg	PO	OD	
	Allopurinol	300mg	PO	OD. **Cycle 1 only.**	

*Note that the use of olanzapine for this purpose of preventing anti-cancer therapy induced nausea and vomiting is unlicensed, this use of olanzapine must be within the treating Trust's governance framework.