Indication	For the treatment of multiple myeloma in patients who have had at least 4 prior lines of systemic therapy and whose disease is refractory to at least 2 proteasome inhibitors, 2 immunomodulatory agents and an antiCD38 monoclonal antibody and which has also demonstrated disease progression on the last therapy. NB not funded for primary amyloidosis.
Treatment Intent	Disease modification
Frequency and number of cycles	Repeat every 7 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 dexamethasone continues or not will be scheduled to occur at least by the end of the second month 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, U&Es and LFTs baseline, weekly for the first 8 weeks of treatment, then every 2 weeks throughout treatment and as clinically indicated. Sodium levels should be corrected prior to initiation of treatment.
	• Baseline body weight, nutritional status and volume check before initiation of treatment, repeated every 2 weeks for the first 8 weeks of treatment 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.
	• **Hepatic impairment**: No dose adjustment of selinexor is required in mild hepatic impairment. There are insufficient data in patients with moderate or severe hepatic impairment to support a dose recommendation.
	• **Renal impairment:** No dose adjustment of selinexor is 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, patients at high risk of TLS should be monitored closely.
	• 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 100mg once weekly, second dose reduction, 80mg once weekly. And third dose reduction, 60mg once weekly. If selinexor is not tolerated at 60mg once weekly treatment should be discontinued. 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.
	• Dehydration due to recurrent diarrhoea or vomiting from selinexor therapy may require dose interruption or modification. Patients should be monitored carefully and electrolyte therapy administered to prevent dehydration in at risk patients.
	• **<u>Common drug interactions (for comprehensive list refer to BNF/SPC)</u>:**
	  ○ **Selinexor:** no formal drug interaction studies have been conducted.
	  ○ Concomitant use of strong CYP3A4 inducer might lead to lower exposure of selinexor.

	• **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. • **Driving and operating machinery:** 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	CDF list accessed online 12.04.2024 SPC accessed online 12.04.2024

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

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.

Repeat every 7 days continuously

TTO	Drug	Dose	Route	Directions
Day 1	**SELINEXOR**	**80mg**	PO	Take **TWICE** a week on day 1 and day 3 at approximately the same time on these days. Swallow whole with water, do not crush, chew or split the tablet. Available as 20mg tablets Supply **7 days' supply only** weeks 1 to 4. From week 5 **14 days'** supply to be given at clinicians discretion.
	DEXAMETHASONE	**20mg**	PO	OM on days 1 and 3. Take with or after food. Take 30minutes before selinexor dose.
	Ondansetron	8mg	PO	BD for 4 days
	Metoclopramide	10mg	PO	Up to TDS PRN Do not take for more than 5 days continuously.
	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.