Indication	First-line treatment of multiple myeloma in patients who are unable to tolerate, or have contraindications to, thalidomide and who are unsuitable for stem cell transplantation. Or For the treatment of multiple myeloma in patients who have received only 1 prior therapy, which included bortezomib. Or For the treatment of multiple myeloma in patients who have received at least 2 prior therapies (NICE TA171), but who are NOT eligible for treatment with the ixazomib + lenalidomide regimen. A formal medical review as to whether treatment with lenalidomide in combination with dexamethasone continues or not will be scheduled to occur at least by the end of the first 8 weeks of treatment.
Treatment Intent	Disease Modification
Frequency and number of cycles	Repeat every 28 days. Continue until progressive disease, unacceptable toxicity or patent's choice, whichever occurs first.
Monitoring Parameters pre-treatment	• **Lenalidomide Prescription Authorisation Form must be completed at time of prescribing** • **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. • U&Es and LFT's on day 1 of each cycle. • FBC on day 1, 8 and 15 for the first 2 cycles and then on day 1 only of each cycle thereafter. • **Thyroid function** at baseline and as clinically indicated throughout treatment. • **<u>Haematological toxicity</u>**: • **First line treatment:** o Treat when neutrophils > 1.0 x 10^9/L and platelets > 50 x 10^9/L. o **Neutropenia:** if neutrophils fall below 0.5 x 10^9/L interrupt treatment and resume at starting dose once resolved to >/=1 x 10^9/L if neutropenia is the only observed toxicity, if other dose dependant haematological toxicities are observed other than neutropenia resume at one reduced dose level when neutrophils have resolved to >/=0.5 x 10^9/L .For each subsequent episode of neutropenia (<0.5 x 10^9/L) interrupt treatment and decrease the dose of lenalidomide to the next dose level when neutrophils have returned to >/=0.5x10^9/L (see table 1). • **Thrombocytopenia:** if platelets fall to <25 x 10^9/L interrupt treatment and resume at one reduced dose level once resolved to >/=50 x 10^9/L. • **Treatment following one prior therapy:** o Treatment must not be started if the ANC <1.0 x 10^9/L, and/or platelet counts <75 x 10^9/L or, dependent on bone marrow infiltration by plasma cells, platelet counts <30 x 10^9/L. o **Neutropenia:** if neutrophils fall below 0.5 x 10^9/L interrupt treatment and resume at original dose once resolved to >/=0.5 x 10^9/L if neutropenia is the only observed toxicity, if other dose dependant haematological toxicities are observed other than neutropenia resume at one reduced dose level when neutrophils have resolved to

	>/=0.5 x 10^9/L. For each subsequent episode of neutropenia (<0.5 x 10^9/L) decrease the dose of lenalidomide to the next dose level (see table 2). Do not dose < 5mg od. ○ **Thrombocytopenia:** if platelets fall below 30 x 10^9/L interrupt treatment and resume at one reduced dose level once resolved to >/=30 x 10^9/L. For each subsequent drop below 30 x 10^9/L interrupt treatment and resume at next lower dose level once returned to >/=30x10^9/L (see table 2). Do not dose < 5mg daily. • **Renal impairment**: • Lenalidomide: No dose reduction required in mild impairment. If CrCl 30-49 ml/min, give 10mg OD, after 2 cycles if the patient is tolerating this dose but not responding to treatment the dose may be escalated to 15mg OD. If CrCl <30ml/min give 15mg on alternate days. If CrCl <30ml/min requiring dialysis give 5mg OD, on dialysis days the dose should be given following dialysis. **NB** an alternative dosing schedule which may be considered, but is not within the licence, is: CrCl 30-50ml/min, give 25mg on alternate days; CrCl <30ml/min, give 25mg twice a week. • Allopurinol: Ensure renal function is normal before prescribing Allopurinol (usual dose is 300 mg od). Reduce Allopurinol dose to 100mg od if CrCl is 10-20ml/min and 100mg on alternate days if CrCl is < 10ml/min. • **Hepatic impairment:** • Lenalidomide has not formally been studied in patients with impaired hepatic function and there are no specific dose recommendations. • **Non-haematological toxicity**: • For Grade 3 or 4 toxicities judged to be related to lenalidomide, treatment should be stopped and only restarted at next lower dose level when toxicity has resolved to ≤ Grade 2 depending on the physician's discretion. • Lenalidomide interruption or discontinuation should be considered for Grade 2 or 3 skin rash. Lenalidomide must be discontinued for angioedema, anaphylactic reaction, Grade 4 rash, exfoliative or bullous rash, or if Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) or Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) is suspected, and should not be resumed following discontinuation from these reactions. • **Steroid toxicity:** • Reduce dose of Dexamethasone to 20mg per dose in elderly patients or those with steroid toxicity– clinical decision. • Treatment with lenalidomide has been associated with an increased risk of venous thromboembolism. All patients should be risk assessed and prophylactic anticoagulation considered. • **Drug interactions:** Lenalidomide may increase digoxin concentration, monitor digoxin levels during treatment. Increased risk of rhabdomyolysis when administered with statins. Combined hormonal contraceptives are predicted to increase the risk of venous thromboembolism when given with Lenalidomide. Manufacturer advises avoid. • **Missed dose:** If less than 12 hours after the usual administration time the patient should take the dose and continue as normal the following day. If more than 12 hours after the usual administration time the dose should be omitted and continue with the schedule the following day. • No treatment breaks of more than 6 weeks beyond the expected cycle length are allowed (to allow any toxicity of current therapy to settle or intercurrent comorbidities to improve).

	• Ensure patient is informed of requirement for strict contraception precautions during treatment with Lenalidomide. Follow Lenalidomide risk management programme. • Pregnancy test – if patient is of child-bearing age (every 4 weeks). • Consider PCP prophylaxis/ antiviral/ antifungal therapy if lymphocyte count <1.0 x 10^9/L • Patients should be advised that lenalidomide can have an effect on their ability to drive and use machines. • For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet.
References	SPC accessed on line 28.09.2023; CDF list v1.137; KMCC proforma HAEM-MYEL-009v1

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

Table 1: Dose reduction for first line treatment:

	Lenalidomide[a]
Starting dose	25 mg
Dose level -1	20 mg
Dose level -2	15 mg
Dose level -3	10 mg
Dose level -4	5 mg
Dose level -5	2.5 mg

Table 2: Dose reduction for treatment following one prior therapy:

Starting dose	25 mg
Dose level -1	15 mg
Dose level -2	10 mg
Dose level -3	5 mg

Repeat every 28 days:

TTO	Drug	Dose	Route	Directions
Day 1	**LENALIDOMIDE**	**25mg**	PO	ON for 3 weeks. The capsules should not be opened, broken or chewed. The capsules should be swallowed whole, preferably with water, either with or without food.
	DEXAMETHASONE	**40mg**	PO	Weekly (Days 1, 8, 15, 22) Take with or after food.
	Omeprazole	20mg	PO	OD
	Allopurinol	300mg	PO	OD for 4 weeks Cycle 1 only
	Metoclopramide	10mg	PO	up to TDS PRN (supply 28 tablets) Do not take for more than 5 days continuously
	Consider prophylactic anticoagulation			
	Consider prophylactic PCP			
	Consider levofloxacin prophylaxis for 12 weeks for all newly diagnosed myeloma patients			