Indication	Lenalidomide maintenance for use in patients with newly diagnosed multiple myeloma who have undergone autologous stem cell transplantation as part of first line treatment. Maintenance Lenalidomide is recommended to start at about day +100 post transplantation. Patients must have had no previous therapy with lenalidomide unless the patient has been: Previously treated with 1st line lenalidomide allowed for transplant eligible patients via the interim treatment change options available during the coronavirus pandemic or The patient has been receiving NHS approved free of charge supply of maintenance lenalidomide as part of the NIHR myeloma XI trial and is due to exit the trial on study closure or The patient has been receiving NHS approved free of charge supply of maintenance lenalidomide as part of the NIHR RADAR trial and whilst still in remission has chosen to exit the trial or The patient chose to self-fund 'top-up' treatment with lenalidomide maintenance prior to now switching to NHS funding as long as he/she started maintenance lenalidomide treatment on or after the 18th February 2020. NB this dosing schedule is currently unlicensed; therefore, clinicians must be mindful of their individual responsibilities when prescribing unlicensed doses.
Treatment Intent	Disease modification
Frequency and number of cycles	Every 28 days. Continue until disease progression, unacceptable toxicity or patient choice to stop treatment. A formal medical review as to whether treatment with lenalidomide should continue or not will be scheduled to occur at least by the end of the first 8 weeks of treatment.
Monitoring Parameters pre-treatment	• **The conditions of the Pregnancy Prevention Programme must be fulfilled and the Lenalidomide Prescription Authorisation Form must be completed at time of prescribing and at each cycle.** • **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. • Monitor FBC at baseline and every 2 weeks for the first 2 cycles, then on day 1 of each cycle. U&Es and LFT's on day 1 of each cycle. • Neuts must be >/=1 and PLT must be >/=100 before starting treatment, exceptions may occur at clinical discretion as in high prognostic risk myeloma the benefit to treat may outweigh the risks. • For each subsequent cycle of treatment neuts must be >/=1.0 and/or platelet counts >/=75. • **Thyroid function** must be assessed at baseline then periodically throughout treatment.

	• Thromboprophylaxis should be based upon individual and myeloma related risks in accordance with IMWG and according to local guidelines. Concomitant administration of erythropoietic agents or previous history of DVT may enhance the risk of thrombotic events. • **Cardiac risks / Congestive Heart Failure (CHF):** Patients with known risk should be closely monitored, and action should be taken to try to minimize all modifiable risk factors (e.g. smoking, hypertension, and hyperlipidaemia). • **Hepatic impairment**: Lenalidomide has not formally been studied in patients with impaired hepatic function and there are no specific dose recommendations. • **Renal impairment:** No dose adjustments are required for patients with mild or moderate (CrCl 30-50mL/min) renal impairment. Not recommended in severe renal impairment (CrCl <30 mL/min, with or without dialysis). • **Carcinogenesis:** In clinical trials of newly diagnosed multiple myeloma, a 4-fold increased incidence of second primary malignancies has been observed in patients receiving lenalidomide. Patients should be carefully evaluated before and during treatment. • **Management of adverse reactions and dose adjustments:** • **Haematological:** Dosing interruption or dose reduction may be required, see table 1. • **Non-haematological:** Lenalidomide is to be permanently discontinued in the event of desquamating/blistering rash of any grade, erythema multiforme =/> grade 3, any rash of grade 4 severity, grade 4 neuropathy or hypersensitivity and grade 3 or higher bradycardia or cardiac arrhythmia. Lenalidomide must be discontinued for angioedema, 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. • Lenalidomide interruption or discontinuation should be considered for Grade 2 or 3 skin rash. • For other Grade 3 or 4 toxicities judged to be related to lenalidomide, treatment should be stopped and only restarted as described in table 2. • If PML is suspected, further dosing must be suspended until PML has been excluded. If PML is confirmed, lenalidomide must be permanently discontinued. • **Dose Modification:** The first recommended dose reduction is to 5mg once daily, if a further dose reduction is required reduce to 5mg every other day. If a patient is unable to tolerate 5mg every other day treatment should be discontinued. • **<u>Common drug interactions (for comprehensive list refer to BNF/SPC)</u>:** 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. • Patients should be advised that lenalidomide can have an effect on their ability to drive and use machines. Patients should be advised it is preferable to take dose at night time. • 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).**

	• 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-044 V2 CDF list V1.318

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

Table 1

Dose modifications for haematological adverse reactions	
Neutropenia: At the physician's discretion, if neutropenia is the only toxicity at any dose level, add granulocyte colony stimulating factor (G-CSF) and maintain the dose level of lenalidomide.	
First fall to <1.0 x 10^9/L	Interrupt lenalidomide treatment. GCSF if Grade 3 with fever or Grade 4.
Return to ≥1.0 x 10^9/L if neutropenia is the only observed toxicity	Resume lenalidomide at starting dose once daily
Return to ≥1.0 x 10^9/L when dose dependent haematological toxicities other than neutropenia are observed	Resume lenalidomide at next lower dose level
For each subsequent drop below 1.0 x 10^9/L	Interrupt lenalidomide treatment. Resume treatment once >1.0 at next lower dose level.
Thrombocytopenia	
First fall to <30 x 10^9/l	Interrupt lenalidomide treatment
Return to ≥30 x 10^9/L	Resume lenalidomide at starting dose
For each subsequent drop below 30 x 10^9/L	Interrupt lenalidomide treatment
Return to ≥30 x 10^9/L	Resume lenalidomide at next lower dose level

Table 2

Dose modifications for non-haematological adverse reactions	
Grade 2 neuropathy with pain or any Grade 3 neuropathy	Hold until ≤ Grade 2. Then resume lenalidomide at reduced dose level
Grade 4 neuropathy	Discontinue
Nausea, vomiting, diarrhoea, dehydration, constipation Grade ≥3 (any duration)	Hold until ≤ Grade 1. Then resume at current dose. For each subsequent event reduce dose level.
Fatigue Grade ≥3 (for any duration)	Hold until ≤ Grade 1. Then resume at current dose. For each subsequent event reduce dose level
Elevation in transaminases (AST and/or ALT) or total bilirubin Grade 3 (for ≥ 5 days) or Grade 4 (for any duration)	Hold until ≤ Grade 1. Then resume at one reduced dose level.
Other non-haematologic toxicity assessed as lenalidomide-related ≥Grade 3	Hold (interrupt) lenalidomide dose. Assess at least weekly. If the toxicity resolves to ≤Grade 1 prior to Day 21, resume at reduced dose level, and continue the cycle until Day 21

Repeat every 28 days.

TTO	Drug	Dose	Route	Directions
Day 1	**LENALIDOMIDE**	**10mg**	PO	ON for 3 weeks, followed by a 7-day break. Swallow whole with water with or without food. Available 10mg and 5 mg capsules.
	Aciclovir	400mg	PO	BD
	Metoclopramide	10mg	PO	3 times a day for 3 days, then 10mg up to 3 times a day as required. Do not take for more than 5 days continuously.
	Aspirin	75mg	PO	OD