Lenalidomide Maintenance Therapy (RVD-Lite)[i]

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
Indicated as single agent maintenance therapy in patients with newly diagnosed multiple myeloma patients who are transplant ineligible after completion of RVD-lite induction and consolidation therapy.	C90	00782a	N/A

* This is for post 2012 indications only.

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Lenalidomide is administered as maintenance treatment, at the discretion of the prescribing consultant, after completion of RVD-Lite induction treatment **(Please refer to NCCP Regimen 00780 Bortezomib, Lenalidomide and dexAMETHasone (RVD-lite) Induction Therapy)** and RVD-Lite consolidation treatment **(Please refer to NCCP Regimen 00781 Bortezomib and Lenalidomide RVD-Lite Consolidation Therapy)**.

Treatment is continued until disease progression or unacceptable toxicity.

Day	Drug	Dose	Route	Cycle
1-21 inclusive	Lenalidomide	15mg	PO[a]	Every 28 days

[a] Lenalidomide capsules should be taken at about the same time each day, in the evening may be preferred due to risk of drowsiness. The capsules should not be opened, broken or chewed. **The capsules should be swallowed whole, preferably with water, either with or without food**. If less than 12 hours has elapsed since missing a dose of lenalidomide, the patient can take the dose.
If more than 12 hours has elapsed since missing a dose at the normal time, the patient should not take the dose, but take the next dose at the normal time on the following day.

ELIGIBILITY:

- Indications as above
- ECOG 0-2

EXCLUSIONS:

- Hypersensitivity to lenalidomide or to any of the excipients
- Grade ≥ 2 peripheral neuropathy
- ANC < 1 x 10^9 cells/L
- Pregnancy
- Patients who are unable to comply with the Lenalidomide Pregnancy Prevention Programme
- Breastfeeding

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Haematologist working in the area of haematological malignancies

TESTS:

Baseline tests:

- FBC, renal, liver and bone profile
- Blood pressure, blood glucose (patients on oral hypoglycaemics)
- Assessment of peripheral neuropathy status
- VTE risk assessment
- Urine pregnancy testing or serum hCG test for women of childbearing potential as per Pregnancy Prevention Programme
- Assessment and registration as per Pregnancy Prevention Program for both male and female patients
- Virology screen - Hepatitis B (HBsAg, HBcoreAb), Hepatitis C and HIV
  ***See Regimen Specific Complications re Hepatitis B Reactivation**

Regular tests:

- FBC; monitor platelet count at a minimum of day 1
- Liver, renal, bone profile
- Blood pressure
- Urine pregnancy testing or serum hCG test every 28 days for women of childbearing potential as per Pregnancy Prevention Programme
- Consider monitoring thyroid function tests
- Blood glucose* if being treated with oral hypoglycaemics **(*See Drug Interactions)**

Disease monitoring:
Disease monitoring should be in line with the patient's treatment plan and any other test(s) as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant
- Lenalidomide treatment must not be started if the ANC is < 1.0 x 10^9/L and/or platelets < 75 x 10^9/L or, dependent on bone marrow infiltration by plasma cells, platelet counts < 30 x 10^9 /L
- Dose level reductions for lenalidomide are described in Table 1 below

Table 1: Dose reduction steps for lenalidomide

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

Haematological:

Table 2: Dose Modifications for Thrombocytopenia

Platelets (x 10^9/L)	Lenalidomide
First Fall to < 30	Interrupt lenalidomide therapy
Return to ≥30	Resume lenalidomide at dose level -1
For each subsequent drop to < 30	Interrupt lenalidomide therapy
Return to ≥30	Resume lenalidomide at next lower dose level once daily. Do not dose below 5mg once daily

Table 3: Dose Modifications for neutropenia

ANC (x 10^9/L)	Lenalidomide
First fall to < 0.5 Return to ≥ 1 (where no other haematological toxicity is observed)	Interrupt lenalidomide therapy Resume lenalidomide at starting dose once daily
Return to ≥ 0.5 (where other haematological toxicity is observed)	Resume lenalidomide at dose level -1
For each subsequent drop to < 0.5	Interrupt lenalidomide therapy
Return to ≥ 0.5	Resume lenalidomide at next lower dose level once daily. Do not dose below 5mg once daily.
In the case of neutropenia, the use of growth factors in patient management should be considered.	
If the dose of lenalidomide was reduced for a haematological dose limiting toxicity (DLT), the dose of lenalidomide may be re-introduced to the next higher dose level (up to the starting dose) at the discretion of the treating consultant if continued lenalidomide/dexAMETHasone therapy resulted in improved bone marrow function (no DLT for at least 2 consecutive cycles and an ANC > 1.5 x 10^9/L with a platelet count > 100 x 10^9/L at the beginning of a new cycle at the current dose level).	

Renal and Hepatic Impairment:

Table 4: Dose modification of Lenalidomide in Renal or Hepatic Impairment

Drug	Renal impairment		Hepatic impairment
Lenalidomide [a]	**CrCl mL/minute**	**Dose modification**	No need for dose adjustment is expected.
	30 to 50	Reduce dose to 10mg once daily[a]	
	<30 not requiring dialysis	15mg every other day	
	< 30 requiring dialysis	5mg once daily. On dialysis days the dose should be administered following dialysis.	
	[a]The dose may be escalated to 15mg once daily after 2 cycles if patient is not responding to treatment and is tolerating the treatment		
[a] Lenalidomide (renal – SPC; hepatic – Giraud et al 2023)			

Dose reductions for other toxicities:

Table 5: Dose Modification of Lenalidomide for Adverse Events

Drug	Adverse reactions*	Recommended dose modification
Lenalidomide	Thromboembolic event	Withhold treatment and start standard anticoagulant therapy. Once stabilised on the anticoagulant therapy and complications of thromboembolic event have been managed, lenalidomide treatment may be restarted at the original dose dependant on a benefit/risk assessment. Anticoagulant therapy should be continued during the course of lenalidomide treatment.
	Skin rash	Withhold treatment and evaluate clinically. If allergic reaction do not resume treatment.
	Angioedema	Discontinue treatment.

*Grading based on NCI Common Toxicity Criteria CTCAE v 4.0

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

- As outlined in NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting link here

Lenalidomide: Minimal to Low (**Refer to local policy**).

For information:

Within NCIS regimens, antiemetics have been standardised by Medical Oncologists and Haemato-oncologists. Information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) - link here
- NCCP Supportive Care Antiemetic Medicines for Inclusion in NCIS (Haemato-oncology) - link here

PREMEDICATIONS: Not usually required. Ensure patient remains well hydrated during treatment.

OTHER SUPPORTIVE CARE:

- In case of neutropenia the consultant may consider the use of growth factors in patient management
- Thromboprophylaxis: Prophylactic antithrombotic medicines should be recommended, especially in patients with additional thrombotic risk factors. Patients should be instructed to seek medical care if they develop symptoms such as shortness of breath, chest pain, arm or leg swelling. Prophylactic antithrombotic medicine options include single agent aspirin, or prophylactic doses of low molecular weight heparin (LMWH) or direct oral anti-coagulant (DOAC) **(Refer to local policy)**
- Both diarrhoea and constipation are common side effects associated with treatment. Patients may require either laxatives or anti-diarrhoeals. **(Refer to local policies)**
- Bisphosphonates should be considered in all patients with myeloma related bone disease
- Tumour Lysis Syndrome prophylaxis (**Refer to local policy**)

ADVERSE EFFECTS:

- Please refer to the relevant Summary of Product Characteristics for details.

REGIMEN SPECIFIC COMPLICATIONS:

- **Hepatitis B Reactivation:** Patients should be tested for both HBsAg and HBcoreAb as per local policy. If either test is positive, such patients should be treated with anti-viral therapy. **(Refer to local infectious disease policy).** These patients should be considered for assessment by hepatology.

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for more information.

COMPANY SUPPORT RESOURCES/Useful Links:

Lenalidomide

- Please refer to the HPRA website (www.hpra.ie) for the individual product for list of relevant support resources
- Prescribers are required to read and understand the relevant HCP Information Guide and to adhere to the PPP

REFERENCES:

1. O'Donnell, K et al. A Phase 2 Study of Modified Lenalidomide, Bortezomib, and Dexamethasone in Transplant-Ineligible Multiple Myeloma – Phase 2 study Br J Haematol. 2018 July
2. Cook et al. Outcomes with different administration schedules of bortezomib in bortezomib, lenalidomide and dexamethasone (VRd) as first-line therapy in multiple myeloma. American Journal of hematology 2020: 26074
3. Giraud E L, Lijster B D, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. Available at: https://pubmed.ncbi.nlm.nih.gov/37269847/
4. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V5 2023. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf
5. Lenalidomide Summary of Product Characteristics EMA. Last updated 08/01/2024. Accessed 29/02/2024. Available at: https://www.ema.europa.eu/en/documents/product-information/revlimid-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	02/11/2022		NCCP Plasma Cell Disorder Clinical Advisory Group
1a	13/02/2024	Updated company support resources/ useful links section in line with NCCP standardisation.	NCCP
2	18/07/2024	Regimen reviewed. Amended Exclusions, Baseline Tests, Other Supportive Care.Updated Tables 3 and 4. Updated Adverse Events/Regimen Specific Complications and Drug Interactions section as per NCCP Standardisation.	Dr Janusz Krawczyk

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

[i] This regimen is outside its licensed indication for the use of lenalidomide in Ireland. Patients should be informed of the unlicensed nature of this indication and consented to treatment in line with the hospital's policy on the use of unlicensed medication and unlicensed or "off label" indications. Prescribers should be aware of their responsibility in communicating any relevant information to the patient and also in ensuring that the unlicensed or "off label" indication has been acknowledged by the hospital's Drugs and Therapeutics Committee, or equivalent, in line with hospital policy.