Lenalidomide Maintenance (Myeloma)

Please note this protocol has been produced in a new format that is currently being piloted. Any feedback on this new format should be sent to SSGMeetings@uhbw.nhs.uk

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Indication

Maintenance treatment in newly diagnosed patients with multiple myeloma who have undergone autologous stem cell transplantation (NICE TA680)

Response Rates

Myeloma XI study:

- 3 year OS: 87.5%
- Median PFS: 39 months (from maintenance to progressive disease)

Regimen details

Day	Drug	Dose	Route
1-21	Lenalidomide	10mg OD*	PO

*Treatment is recommended to start at about day 100 following consolidation.

Cycle frequency

28 days

Number of cycles

Continuous until disease progression or unacceptable toxicity or patient choice, whichever sooner.

Pre-medication

Nil

Supportive medication

Thromboprophylaxis is required unless contraindicated. Patients should be risk assessed for underlying risk factors for VTE and treated with appropriate thromboprophylaxis. Recommend aspirin 75mg daily for low risk (lower disease burden and induction) or apixaban 2.5mg BD for high risk.
Antiviral prophylaxis as per local policy and post autologous transplant policy.
Pneumocystis jirovecii pneumonia (PJP) as per local policy and post autologous transplant policy.
Bisphosphonates as per SWAG 'Bone Protection Myeloma' protocol

Emetogenicity

This regimen has low emetogenic potential. Routine anti-emetic is not required.

Administration

Lenalidomide capsules are available in various strengths. For maintenance 10mg should be used with 5mg for dose reductions. Lenalidomide should be swallowed whole with water, either with or without food, at the same time each day and should not be broken, opened or chewed. If a dose is missed it may be taken within 12 hours, however if more than 12 hours has elapsed since the dose was due, the patient should miss the dose and resume the usual dose the next day.

Lenalidomide must be prescribed and dispensed in accordance with the pregnancy prevention programme.

Extravasation

N/A

Mandatory investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+Es (including creatinine)	14 days
LFTs	14 days
Pregnancy test, in women of childbearing age	3 days

Additional investigations advised pre-first cycle

Other recommended investigations:
Virology (Hep B/C, HIV)
Serum calcium
Serum protein electrophoresis
Serum free light chains (SFLC)/Paraprotein (PP)/Immunoglobulins (Igs)

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	7 days
U+Es (including creatinine)	7 days
LFTs	7 days
Pregnancy test, in women of childbearing age	3 days

Additional investigations advised pre subsequent cycles

Serum calcium
Serum protein electrophoresis
Serum free light chains (SFLC)/Paraprotein (PP)/Immunoglobulins (Igs)

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer must be given by prescriber/ consultant

Investigation	Limit
Neutrophils	≥ 1.0 x 10^9/L
Platelets	≥ 75 x 10^9/L
Creatinine clearance	≥ 30mL/min
ALT	≤ 1.5 ULN
Bilirubin	≤ 3 x ULN

Dose modifications

Dose adjustments are made as per the table below.

Lenalidomide dose level	Lenalidomide dose
Starting dose	10mg
Dose level -1	5mg
Dose level -2	5mg every other day
Dose level -3	Discontinue

These are as per the Myeloma XI trial protocol (v9.0 Nov 2017) and not the SPC.

If lenalidomide was omitted during the previous cycle, or if the new cycle is delayed due to toxicity, then the new cycle will be started with a one-level dose reduction.

Haematological toxicity

Treatment should only be initiated if neutrophils ≥ 1.0 x 10^9/L and platelets ≥ 75 x 10^9/L (if bone marrow infiltration may initiate treatment if platelets ≥ 30 x 10^9/L). If neutrophil and/or platelet count is not met on day 1 of a new cycle, patient should be evaluated weekly and a new treatment cycle will not be initiated until toxicity has resolved.

Thrombocytopenia

Platelet count	Action
<30 x 10^9/L (First occurrence)	Interrupt lenalidomide treatment Resume lenalidomide at starting dose for that cycle once platelets ≥30 x 10^9/L
<30 x 10^9/L (Subsequent occurrence)	Interrupt lenalidomide treatment Resume lenalidomide at next lower dose level once platelets ≥30 x 10^9/L

Neutropenia

Neutrophil count	Action
<1.0 x 10^9/L (First occurrence)	Interrupt lenalidomide treatment. Give GCSF if grade 3 (neutrophils 0.5-1 x 10^9/L) with fever or grade 4 (neutrophils <0.5 x 10^9/L). Resume lenalidomide at starting dose for that cycle once neutrophils ≥1.0 x 10^9/L
<1.0 x 10^9/L (Subsequent occurrence)	Interrupt lenalidomide treatment. Resume lenalidomide at next lower dose level once neutrophils ≥1.0 x 10^9/L

Renal impairment

Creatinine Clearance (CrCl)	Lenalidomide dose
<30mL/min (without dialysis)	5mg OD
<30mL/min (with dialysis)	5mg alternate days

Hepatic impairment

Lenalidomide has not been studied in patients with impaired hepatic function and there are no recommendations in terms of dosing. If patients suffer unexplained deterioration of liver function, consider lenalidomide induced liver injury. In this case liver function should improve on discontinuation of lenalidomide.

Bilirubin		AST/ALT	Lenalidomide dose
≥ 3 x ULN (for ≥5 days)	or	AST/ALT ≥ 5 x ULN (for ≥5 days)	Hold until ≤1.5 x ULN. Then resume at next lower dose level
≥ 10 x ULN (any duration)	or	AST/ALT ≥ 20 x ULN (any duration)	Hold until ≤1.5 x ULN. Then resume at next lower dose level

Other toxicities

Toxicity	Definition	Dose adjustment
Neuropathy	Grade 2 with pain or any grade 3	Hold until ≤ grade 2; Resume at reduced dose level.
	Grade 4	Discontinue
Nausea, vomiting, diarrhoea, constipation, dehydration	≥ grade 3	If symptoms persist despite maximal supportive therapy, interrupt lenalidomide until ≤ grade 1 then resume at current dose. For each subsequent event, reduce dose level.
Congestive heart failure	Any symptoms, whether or not drug related.	Interrupt treatment until resolution; After resolution continue treatment at reduced dose level.
Fatigue	≥ grade 3	Interrupt lenalidomide until ≤ grade 1 then resume at current dose. For each subsequent event, reduce dose level.
Rash	Grade 2 or 3	Other causes for rash (e.g. co-trimoxazole) should be ruled out. Treatment of the rash can include topical steroids and emollients, in addition to antihistamines. Interrupt lenalidomide treatment if indicated. If rash resolves resume at next lower dose level.
	Grade 4 or angioedema, anaphylactic reaction, exfoliative or bullous rash, or Stevens-Johnson	Discontinue lenalidomide

	syndrome (SJS), toxic epidermal necrolysis (TEN) or Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) is suspected	
Other non-haematological toxicity	≥ grade 3	Interrupt lenalidomide. Assess at least weekly. If toxicity resolves to ≤ grade 1 prior to day 21, resume at reduced dose level and continue the cycle until day 21.

Thrombosis:
If a patient experiences a thromboembolic event, treatment with lenalidomide must be discontinued and anticoagulation therapy commenced. Once the patient has been stabilised on anticoagulation treatment and any complications of the thromboembolic event have been managed, lenalidomide may be restarted at the original dose, after a reassessment of risks and benefits of treatment.

Side Effects

Myeloma XI study:

Toxicity		**Any grade (%)**	**Grade 3 or 4 (%)**
Haematological	Neutropenia	38	33
	Thrombocytopenia	45	6
	Anaemia	60	5
Non-haematological	Fatigue or lethargy	33	1
	Peripheral sensory neuropathy	29	1
	Constipation	28	<1
	Respiratory infections	24	9
	Back pain	16	<1
	Rash	14	1
	Nausea	13	<1
	Cough	13	<1
	Sepsis	<1	2
	Myalgia	12	<1
	Arthralgia	10	<1
	Infections and infestations	9	2
	Sepsis	<1	2

Specific drug related side effects:

Lenalidomide

Common (>10%)	**Uncommon (1-10%)**	**Rare (<1%)**
Infection	Dry mouth	PML
Bruising or bleeding	Peripheral neuropathy	TLS
Constipation or diarrhoea	VTE	Impotence
Skin rash (see below)	Poor appetite	
Taste changes	Hypothyroidism	
Dizziness/hypotension	Tinnitus	
Bile salt malabsorption (see below)	Loss of appetite/weight loss	

*Teratogenicity	Secondary primary malignancies	

*the pregnancy prevention programme should mitigate this risk

- **Skin rash**

Other causes for rash (e.g. co-trimoxazole) should be ruled out. Treatment of the rash can include topical steroids and emollients, in addition to antihistamines.

- **Bile salt malabsorption**

Bile salt malabsorption (BSM) is a relatively common side effect of lenalidomide therapy and can occur at any time during therapy. It tends to present with symptoms of diarrhoea, urgency and on occasions, incontinence. It is treated with the addition of bile salt sequestrants (e.g. cholestyramine 4g od, colesevelam 1.25-3.75g/day in 2-3 divided doses) with the dose being titrated according to symptoms. Screening for vitamin B12 deficiency is also advised as this can be a recognised complication of BSM.

- **Thrombosis**

If a patient experiences a thromboembolic event treatment with anticoagulation therapy should be initiated and the lenalidomide continued.

- **Pregnancy Prevention**

The conditions of the Lenalidomide Pregnancy Prevention Programme must be fulfilled for all male and female patients. All women of childbearing potential must use one effective method of pregnancy prevention at least 4 weeks before therapy, during therapy and for at least 4 weeks after stopping therapy. Men are required to use a barrier method of contraception during treatment.

Additional information

N/A

Significant drug interactions – for full details consult product literature/ reference texts

Erythropoietic agents: increased risk of thrombosis – use with caution in patients with high risk to VTE
Hormone treatments (including combined contraceptive pill, HRT): increased risk of thrombosis – use with caution in patients with high risk to VTE
Digoxin: may increase plasma digoxin levels – monitor levels
Statins: increased risk of rhabdomyolysis when statins are administered with lenalidomide

References

- National Institute for Health and Care Excellence (NICE), TA680. Accessed: 26th November 2025 via www.nice.org.uk
- Summary of Product Characteristics – Lenalidomide (Amarox Limited) accessed 26th November 2025 via www.medicines.org.uk
- Jackson, GH et al. Lenalidomide maintenance versus observation for patients with newly diagnosed multiple myeloma (Myeloma XI): a multicentre, open-lael, randomised, phase 3 trial. Lancet Oncology, 2019: 20 (1):57-73
- Myeloma XI clinical trial protocol EudraCT Number 2009-010956-93 version 9.0 2nd November 2017

Version	Issue date	Review date	Revision	Written/Checked/Authorised
1	May 2021	May 2024	New protocol	Written: Becky Bagnall (Pharmacist, North Bristol NHS Trust) and Alastair Whiteway (Consultant Haematologist, North Bristol NHS Trust) Checked: Kate Gregory (Lead Pharmacist for SACT protocols, SWAG Cancer Alliance) Authorised: Dr Jeremy Braybrooke (Consultant Oncologist, UHBW NHS Trust and SWAG Cancer Alliance)
2	17/12/2025	December 2027	Transfer to new template. Blood validity period and limits to proceed updated.	Written: Dr S Moore (Consultant Haematologist, UHBW NHS Trust) Checked: Anna Wong (Lead Pharmacist for Haematology SACT Protocols, SWAG Cancer Alliance) Authorised: Dr J Braybrooke (Consultant Oncologist, UHBW NHS Trust and SWAG Cancer Alliance)