Systemic Anti Cancer Therapy Protocol

Maintenance Lenalidomide after Autologous Stem Cell Transplant
Multiple Myeloma

PROTOCOL REF: MPHAMLASHA
(Version No: 1.0)

Approved for use in:

- Patients with newly diagnosed multiple myeloma who have undergone autologous stem cell transplantation
- Patients must not have previously been treated with lenalidomide, unless via the interim treatment change options available during the coronavirus pandemic
- Treatment should start around 100 days after stem cell transplantation and continued until disease progression or unacceptable toxicity

Blueteq registration required: see blueteq for further eligibility criteria

Dosage:

Drug	Dose	Route	Frequency
Lenalidomide	**10mg ONCE daily**	PO	Days 1-21

Cycle **every 28 days** – treatment to be continued until disease progression or intolerance

Please note that dosing is based on the Myeloma XI trial rather than on the marketing authorisation of Revlimid

Administration and Counselling Points:

- Lenalidomide capsules should be taken orally at about the same time on the scheduled days. The capsules should not be opened, broken or chewed. The capsules should be swallowed whole, preferably with water, either with or without food.
- If dose is missed and <12hours late the missed dose should be taken. Missed doses >12hours should be omitted and the next dose taken as scheduled.
- The prescriber must inform male and female patients about the expected teratogenic risk and the strict pregnancy prevention measures as specified in the pregnancy prevention programme and provide patients with appropriate patient educational brochure and patient card.

Emetogenic risk:

Low risk

Supportive treatments:

Anticoagulation – options include prophylactic dose of low molecular weight heparin (LWMH), treatment dose of LMWH in high risk patients. For patients established on DOACs, patients may continue DOAC treatment or be switched to a LMWH. For those patients who decline LMWHs or for those deemed to be low risk on long term treatment – there is the option to be converted to aspirin after having LMWH in the first 6-12 months

The following are optional additional supportive medicines only to be prescribed if deemed necessary:

- Ondansetron 4mg-8mg TDS prn for 5-7 days
- Aciclovir 400mg BD
- Co-trimoxazole 480mg OD
- Nystatin 1mL QDS

Interactions:

Lenalidomide:

- Agents that may increase the risk of thrombosis, such as HRT should be used with caution in multiple myeloma patients receiving lenalidomide with dexamethasone.
- **Digoxin** – concomitant administration with lenalidomide increased plasma exposure of digoxin, monitoring of the digoxin concentration is advised during lenalidomide treatment.
- **Statins** – there is an increased risk of rhabdomyolysis when statins are administered with lenalidomide. Enhanced clinical and laboratory monitoring is warranted notably during the first weeks of treatment.

Please refer to the relevant SPC for more drug-drug interaction information.

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2	Ongoing
Informed Consent	X			
Clinical Assessment	X	X	X	
SACT Assessment (including toxicities and performance status)		X	X	
FBC	X	X	X	
Celgene Pregnancy Prevention Program Consent	X			
Celgene prescription authorization form		X	X	
U&E & LFTs	X	X	X	
CrCl (Cockcroft and Gault)	X			
Bone profile	X			As clinically indicated
Dental assessment	X			As clinically indicated
Serum Igs/electrophoresis/serum free light chains (if indicated)	X	X	X	Prior to every cycle
Neurological assessment (for neuropathy)	X	X	X	Prior to every cycle
Imaging as per NICE/network guidance and clinical indication	X			To restage as indicated
Pregnancy test	X			If clinically indicated
Height	X			
Weight	X	X	X	Prior to every cycle

Dose Modifications and Toxicity Management:

Dose step reductions:

	Lenalidomide
Starting dose	10mg
Dose level 1	5mg or (10mg alternate days to finish course)
Dose level 2	5mg alternate days
Dose level 3	Discontinue

Haematological toxicity:

Maintenance treatment should only be started when:

Neutrophil count is ≥1.0 x 10^9/L and platelets ≥100 x 10^9/L.

For each subsequent cycle of treatment, lenalidomide should not be started if the neutrophil count <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.

Thrombocytopenia:

When platelets	**Recommended course**
First fall to < 30 x 10^9/L	Interrupt treatment
First return to ≥ 30 x 10^9/L	Restart treatment at starting dose
Subsequent falls to <30 x10^9/L	Interrupt treatment
Subsequent returns to ≥ 30 x 10^9/L	Restart treatment at next lowest dose level

Neutropenia:

When neutrophils	**Recommended course**
First fall to <1 x 10^9/L	Interrupt lenalidomide treatment
Return to ≥ 1.0 x 10^9/L when neutropenia is the only observed toxicity	Resume lenalidomide at starting dose once daily
Return to ≥ 1 x 10^9/L when dose-dependent haematological toxicities other than neutropenia are observed	Resume lenalidomide at next lowest dose level
For each subsequent drop below < 1 x 10^9/L	Interrupt lenalidomide treatment
Return to ≥ 1 x 10^9/L	Resume lenalidomide at next lower dose level once daily.

Dosing in renal and hepatic impairment:

Renal	No dose adjustments are required for patients with mild and moderate renal impairment and multiple myeloma. Lenalidomide should not be used in patients with severe (CrCl <30ml/min) renal impairment.

Hepatic	Lenalidomide has not formally been studied in patients with impaired hepatic function and there are no specific dose recommendations.

Non- Haematological toxicity:

Toxicity	Recommendation
Non-blistering rash Grade 3 Grade 4	Hold (interrupt) lenalidomide dose; follow up weekly. If the toxicity resolves to ≤ Grade 1 prior to Day 21, resume at next lower dose level (5 mg less) and continue the cycle until Day 21. Discontinue
Desquamating (blistering) rash Any Grade	 Discontinue
Erythema multiforme ≥Grade 3	 Discontinue
Sinus bradycardia/ other cardiac arrhythmia Grade 2 Grade 3+	 Hold (interrupt) lenalidomide dose; follow up weekly. If the toxicity resolves to ≤ Grade 1 prior to Day 21, resume at next lower dose level (5 mg less) and continue the cycle until Day 21. Discontinue
Allergic reaction/ hypersentivity Grade 2 or 3 Grade 4	 Hold (interrupt) lenalidomide dose; follow up weekly. If the toxicity resolves to ≤ Grade 1 prior to Day 21, resume at next lower dose level (5 mg less) and continue the cycle until Day 21. Discontinue
Venous thrombosis/embolism ≥ Grade 3	 Hold (interrupt) lenalidomide dose and start anticoagulation; resume at investigator's discretion (maintain dose level).

Hyperthyroidism or hypothyroidism	Omit lenalidomide for remainder of cycle, evaluate aetiology, and initiate appropriate therapy.
Infection Grade 3 or 4	Hold lenalidomide until systemic treatment for infection is completed. If no neutropenia, resume both drugs at current dose. If neutropenic, follow neutropenic instructions.
Herpes Zoster any grade or Herpes Simplex	Hold both lenalidomide until lesions are dry. Resume at current doses
Grade 2 neuropathy with pain or **Grade 3 neuropathy**	Hold until ≤ Grade 2. Then resume lenalidomide at reduced dose level
Grade 4 neuropathy	Discontinue
Congestive Heart Failure (CHF)	Any subject with symptoms of CHF, whether or not drug related, must have the dose held until resolution of the CHF. After the CHF has resolved or returned to baseline, treatment may continue at a reduced dose, at the discretion of the treating clinician. If there is no resolution of CHF after 2 weeks, the subject should be withdrawn from treatment.
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 Grade ≥3	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.

References:

1. Summary of Product Characteristics, Revlimid®, Lenalidomide, Celgene, last updated 30/11/2020 https://www.medicines.org.uk/emc
2. NICE [GID-TAG430] – Multiple myeloma – lenalidomide (maintenance, post autologous stem cell transplantation). Expected to be published: 3 March 2021 www.nice.org.uk [accessed on 2021]
3. Myeloma XI trial protocol v9 (2/11/17). EudraCT number: 2009-010956-93