Lenalidomide Maintenance

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

ICD-10 codes
Codes with a pre-fix C90

Regimen details

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

Treatment is recommended to start at about day 100 after stem cell transplantation.

*Note: Dosing is as per the Myeloma XI protocol version 9.0 (November 2017). This dosing schedule is not the licensed one as set out in the Lenalidomide Summary of Product Characteristics but is the one on which NICE assessed the clinical and cost effectiveness of maintenance Lenalidomide and is the stipulated dosing schedule for NICE funding.

Cycle frequency
28 days

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

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.
The capsules 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.

Pre-medication
Nil

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

Additional supportive medication
Thromboprophylaxis is required unless contraindicated. Patients should be risk assessed for underlying risk factors for VTE (e.g. Myeloma Academy risk scoring system) and treated with appropriate thromboprophylaxis. Suggested aspirin (75mg daily) for low risk, LMWH for high risk.
Bisphosphonates as per local policy
Antifungal, antiviral and antibiotic/PCP prophylaxis as per local policy and post autologous transplant policy.

Extravasation

N/A

Investigations – pre first cycle

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

Hepatitis B virus status should be established before initiating treatment with lenalidomide.

Other recommended investigations:
Serum calcium
Serum protein electrophoresis (or alternative measure of response if M protein not measurable).
Baseline thyroid function

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	Weekly for first 8 weeks, then 7 days before subsequent cycles
U+Es (including creatinine)	7 days
LFTs	7 days
Pregnancy test, in women of childbearing age	3 days

Other recommended investigations:
Serum calcium.
Serum electrophoresis (or alternative measure of response if M protein not measurable).
Intermittent monitoring of thyroid function.

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	≤ 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 halted during the previous cycle and was restarted with a dose reduction, without requiring an interruption for the remainder of the cycle, that reduced level will be initiated on day 1 of the new cycle.

If lenalidomide was omitted for the remainder of the previous cycle, or if the new cycle is delayed due to toxicity encountered on schedule day, 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, no other haematological toxicity)	Interrupt lenalidomide treatment. Give GCSF if grade 3 with fever or grade 4. Resume lenalidomide at starting dose for that cycle once neutrophils ≥1.0 x 10^9/L
<1.0 x 10^9/L (first occurrence, plus other dose-dependent haematological toxicity)	Interrupt lenalidomide treatment. Resume lenalidomide at next lower dose level 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	**Lenalidomide dose**
≥30ml/min	No dose adjustment required
<30ml/min (with or without dialysis)	Discontinue lenalidomide

- **Hepatic impairment**

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
Neuropathy	Grade 4	Discontinue
Nausea, vomiting, diarrhoea, constipation, dehydration	≥ grade 3	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, treatment may be continued at reduced dose level.
Fatigue	≥ grade 3	Interrupt lenalidomide until ≤ grade 1 then resume at current dose. For each subsequent event, reduce dose level.
Other non-haematologic 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.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Pneumonia/lung infection
Myelosuppression
Teratogenicity (contraindicated unless all of the conditions of the Pregnancy Prevention Programme are met)
Venous thromboembolism
Pulmonary hypertension
Viral reactivation in patients previously infected with the varicella zoster or hepatitis B viruses (HBV).
Myocardial infarction/arterial thromboembolism
Thyroid disorders
Allergic reactions and severe skin reactions
Progressive multifocal leukoencephalopathy (mainly reported in patients taking concomitant steroids)
Second primary malignancies

- **Frequently occurring side effects**

Myelosuppression
Constipation, diarrhoea
Nausea and vomiting
Fatigue

- **Other side effects**

Reduced appetite
Altered LFTs
Peripheral neuropathy

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

Additional comments

The conditions of the Lenalidomide Pregnancy Prevention Programme must be fulfilled for all male and female patients. Prescribing and dispensing of lenalidomide must be in line with the Pregnancy Prevention Programme. All women of child bearing 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.

References

- Summary of Product Characteristics: Lenalidomide (Celgene) accessed 11/02/2021 via https://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
- National Cancer Drugs Fund List accessed 11/02/2021 via https://www.england.nhs.uk/cancer/cdf/cancer-drugs-fund-list/
- Re: Lenalidomide Maintenance in multiple myeloma: NICE Guidance UKMF statement 5 February 2020 https://www.ukmf.org.uk/guidelines-page/bshukmf-guidelines/

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