Lenalidomide and dexamethasone

Indication

Treatment of multiple myeloma in patients who have received two or more previous therapies.

For patients who receive more than 26 cycles, the cost of any subsequent cycles will be met by the manufacturer.

(NICE TA171)

ICD-10 codes

Codes with a pre-fix C90

Regimen details

Day	Drug	Dose	Route
1-21	Lenalidomide	25mg OD	PO
1-4, 9-12 and 17-20 (for first 4 cycles, then modified based on clinical findings)	Dexamethasone*	40mg OM	PO

* Less intense dexamethasone dosing may be used for patients who are unsuitable for the above regimen, based on age, disease or previous tolerability.

Options include:

- Dexamethasone 20-40mg OM days 1-4 with additional 4 day pulses if required at the start of treatment (days 8-11, 15-18)

OR

- Dexamethasone 20-40mg OM weekly on days 1,8,15 and 22

Cycle frequency

28 days

Number of cycles

Until disease progression or unacceptable toxicity

Administration

Lenalidomide is available as 5mg, 10mg, 15mg, 20mg and 25mg capsules.

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 with the usual dose the next day.

Lenalidomide must be prescribed and dispensed in accordance with the pregnancy prevention programme. A prescription authorisation form is required for each dispensing (paper or electronic, depending on local practice).

Dexamethasone is available as 500microgram and 2mg tablets. The dose should be taken in the morning, with or after food.

Pre-medication
Nil

Emetogenicity
This regimen has mild emetogenic potential. Routine antiemetics are not usually required.

Additional supportive medication
Thromboprophylaxis is required unless contraindicated. Aspirin is appropriate for patients who have no additional risk factors. For patients with additional thromboembolic risk factors (such as immobility, dexamethasone >20mg/day) a low molecular weight heparin is recommended for the first 4 cycles. It may then be appropriate to switch to aspirin.
H_2 antagonist or proton pump inhibitor
Allopurinol 300mg OD (100mg OD if CrCl< 20mL/min) for patients with a high tumour burden, for the first cycle only
Bisphosphonates as per local policy
Antifungal, antiviral and PCP prophylaxis as per local policy

Extravasation
N/A

Investigations – pre first cycle

Investigation	Validity period
FBC and clotting screen	7 days
U+Es (including creatinine)	7 days
LFTs	7 days
Glucose	7 days
Calcium	7 days
Pregnancy test	3 days
Serum electrophoresis (or alternative biological measure of response if M protein not measurable)	

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

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	Weekly for first 8 weeks, then monthly within 72 hours of next cycle
U+Es (including creatinine)	Monthly within 72 hours of next cycle
LFTs	Monthly within 72 hours of next cycle
Calcium	Monthly within 72 hours of next cycle
Glucose	As clinically indicated whilst taking dexamethasone
Blood pressure	As clinically indicated whilst taking dexamethasone
Pregnancy test	Within 3 days of next cycle

Serum electrophoresis (or alternative biological measure of response if M protein not measurable)

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
Haemoglobin	≥ 100 g/L
Creatinine clearance	≥ 50mL/min

Dose modifications

Dose adjustments for lenalidomide are made as per the table below:

Starting dose	25mg
Dose level - 1	15mg
Dose level - 2	10mg
Dose level - 3	5mg

Alternative dose adjustments may include keeping at the same dose and reducing to an alternate day regimen.

- **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).

Subsequent cycles:

Thrombocytopenia

Platelets (x 10^9/L)	**Action**
< 30 (1st occurrence)	Withhold lenalidomide Once recovered to ≥ 30 x 10^9/L continue at dose level - 1
< 30 (2nd occurrence)	Withhold lenalidomide Once recovered to ≥ 30 x 10^9/L continue at dose level - 2
< 30 (3rd occurrence)	Withhold lenalidomide Once recovered to ≥ 30 x 10^9/L continue at dose level – 3 Dose should not be reduced to less than 5mg daily

Neutropenia

Neutrophils (x 10^9/L)	**Action**
< 0.5 (1st occurrence)	Withhold lenalidomide If neutropenia is only toxicity: once recovered to ≥ 0.5 x 10^9/L continue at full starting dose If other dose dependent haematological toxicity: once recovered to ≥ 0.5 x 10^9/L continue at dose level - 1
< 0.5 (2nd occurrence)	Withhold lenalidomide Once recovered to ≥ 0.5 x 10^9/L continue at dose level - 2
< 0.5 (3rd occurrence)	Withhold lenalidomide Once recovered to ≥ 0.5 x 10^9/L continue at dose level – 3 Dose should not be reduced to less than 5mg daily

- **Renal impairment**

Lenalidomide is excreted via the kidney. Close monitoring of renal function is essential.

CrCl (mL/min)	**Lenalidomide dose**
≥ 50	25mg OD
30-49	10mg OD (may escalate to 15mg OD after 2 cycles if patient not responding but is tolerating treatment)
< 30 (not requiring dialysis)	15mg alternate days (may escalate to 10mg OD if patient tolerating treatment)
< 30 (requiring dialysis)	5mg OD (taken after dialysis on dialysis days)

- **Hepatic impairment**

Lenalidomide has not been studied in hepatic impairment. There are no dose recommendations in hepatic impairment.

If patients suffer unexplained deterioration of liver function, consider lenalidomide induced liver injury. In this case liver function should improve on discontinuation of lenalidomide.

- **Other toxicities**

For any grade 3 or 4 non-haematological toxicity (except alopecia), clinical judgement should determine whether to discontinue treatment or to continue treatment at a reduced dose (following recovery to ≤ grade 2 toxicity). Refer to dose reduction table above for dosing guidance. Consultant decision.

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.

Steroid side effects:
For any severe steroid-related side effect, consider alternative steroid dosing (as per regimen details above).

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

- **Serious side effects**

Myelosuppression
Teratogenicity
Venous thromboembolism
Psychosis
Viral reactivation in patients previously infected with the varicella zoster or hepatitis B viruses (HBV).

- **Frequently occurring side effects**

Myelosuppression
Constipation, diarrhoea
Nausea and vomiting
Fatigue
Peripheral neuropathy
Sleep disturbance
Insomnia
High blood sugars
Fluid retention
Dyspepsia

- **Other side effects**

Reduced appetite
Blurred vision
Altered LFTs

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

Erythropoetic agents: increased risk of thrombosis – use with caution

Hormone treatments (including combined contraceptive pill, HRT) : increased risk of thrombosis – use with caution

Digoxin: may increase plasma digoxin levels – monitor levels

Additional comments

References

- Summary of Product Characteristics: Lenalidomide (Celgene) accessed 29 July 2015 via www.medicines.org.uk
- National Institute for Clinical Excellence. Technology Appraisal Guidance 171. Accessed 29 July 2015 via www.nice.org.uk
- Weber DM et al. Multiple Myeloma (009) Study Investigators. Lenalidomide plus dexamethasone for relapsed multiple myeloma in North America. NEJM. 2007;357(21):2133-2142
- Dimopoulos M et al. multiple Myeloma (010) Study Investigators. Lenalidomide plus dexamethasone for relapsed or refractory multiple myeloma. NEJM.2007;357 (21):2123-2132
- https://assets.publishing.service.gov.uk/media/584e872440f0b60e4a00007d/Revlimid_DHPC_UK_FINAL.pdf

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