Lenalidomide & Dexamethasone +/- Cyclophosphamide (LCD)

Lenalidomide may be used in combination with dexamethasone for the treatment of multiple myeloma in patients who have received at least 2 prior therapies – NICE approved 2009

All patients should be screened for hepatitis B virus before starting treatment
This screen must include HBV surface antigen and anti-HBV core antibody

Drugs/Doses:

Lenalidomide 25mg po once daily on Days 1 – 21, followed by 7 days rest

Dexamethasone† 20 – 40*mg po once weekly on Days 1, 8, 15 & 22

+/- (do not include in patients with cytopenias):

Cyclophosphamide 500mg po once weekly on Days 1, 8 and 15

† Or "pulsed" dexamethasone may be used if there is a need for rapid cytoreduction:
20 – 40*mg po once daily in the morning on days 1 to 4, +/- additional 4-day pulses on days 8 to 11 +/- days 15 to 18 of each cycle

* dexamethasone dose may be chosen according to age of patient, disease burden and prior tolerability

Other drugs:

Consider allopurinol - dose according to renal function - for the first four weeks (may be omitted in the context of treatment change in patients with good haematological disease control)
Laxative as required for lenalidomide-induced constipation.
The following are recommended, while treating with steroid +/- cyclophosphamide:

- Omeprazole 20mg po od (or ranitidine)
- Fluconazole 100mg po od for antifungal prophylaxis.
- Thromboprophylaxis, according to unit practice, in the absence of specific contraindication.
  The duration of thromboprophylaxis should be guided by risk factors such as active disease (e.g. for the first 4–6 months of treatment until disease control achieved), and then de-escalated or discontinued unless there are ongoing significant risk factors.
- Consider PCP prophylaxis – prescribe according to unit practice

Administration:

Lenalidomide is available as 5mg, 10mg, 15mg and 25mg capsules.
The daily dose should be swallowed whole with water, with or without food, at the same time of day each day.
Dexamethasone to be taken in the morning with or after food.
Cyclophosphamide available as 50mg tablets, to be swallowed whole with a full glass of water.
Encourage 2 – 3 litres oral fluid intake over the 24 hours after each dose, to reduce the risk of haemorrhagic cystitis.

Frequency:

28 day cycle with lenalidomide taken on Days 1 – 21, followed by a 7-day rest.
Dexamethasone and cyclophosphamide for up to 6 - 8 cycles, to maximum response.
Lenalidomide maintenance to continue until disease progression or unacceptable toxicity.
If the patient is still receiving treatment after 26 cycles (normally 2 years), all further lenalidomide drug costs after that time will be met by the manufacturer. (Pharmacy to ensure that a claim is made with the manufacturer)

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Prepared by: S Taylor	Checked by: C Tucker

Main Toxicities:	teratogenicity (see Comments); myelosuppression; muscle cramps; constipation or diarrhoea; rash; increased risk of thromboembolic events; haemorrhagic cystitis, if cyclophosphamide included	
Regular Investigations:	FBC	every week for the 1st 8 weeks, then monthly
	LFTs	every week for the 1st 8 weeks, then monthly
	U&Es	every month
	Paraprotein and/or serum free light chains	every 4 weeks
	Pregnancy test	every month for women of child bearing potential
	Blood glucose	see Comments
	Blood pressure	see Comments

Comments:

Lenalidomide is structurally related to thalidomide, so is expected to be teratogenic. Women of child bearing potential must have a negative pregnancy test within 3 days prior to starting treatment, and within 3 days of each prescription. Pregnancy testing should be repeated monthly thereafter until one month after stopping lenalidomide (or every 2 weeks in women with irregular menstrual cycles). If a woman taking lenalidomide thinks she may be pregnant she must stop the drug immediately.

Women of child-bearing potential must use one agreed effective method of contraception for at least 4 weeks before starting lenalidomide, while on lenalidomide and for one month after. (The combined oral contraceptive pill is not recommended due to the increased risk of thromboembolism.) Men taking lenalidomide must use a barrier method of contraception throughout treatment and for one week after stopping, if their partner is capable of bearing children.

Lenalidomide is supplied through a Pregnancy Prevention Programme. All aspects of the programme should be followed, including completion of an authorisation form by both doctor and pharmacist with every cycle.

While on dexamethasone, blood glucose and blood pressure monitoring to be tailored according to individual patient needs.

Dose Modifications

Haematological Toxicity:

Pre Cycle 1:
If neutrophils < 1.0 x 10^9/L or platelets < 75 x 10^9/L, do not start treatment.
(if bone marrow infiltration, may initiate treatment if platelets ≥ 30 x 10^9/L)

At weekly FBC for 1st 8 weeks, then before subsequent cycles (for patients who start at 25mg dose):

Neutrophils < 0.5 x 10^9/L	Interrupt treatment. Once recovered to ≥ 0.5 x 10^9/L, re-start treatment with dosing of lenalidomide as follows:
First occasion:	if neutropenia was the only observed toxicity, restart at 25mg daily dose. However, if any other dose-dependent haematological toxicity also observed, resume at 15mg daily dose*.
Second and subsequent occasions:	resume with a one step dose reduction (from 25mg to 15mg daily; from 15mg to 10mg daily; from 10mg to 5mg daily)*

Platelets < 30 x 10^9/L	Interrupt treatment. Once recovered to ≥ 30 x 10^9/L, re-start treatment*, with dosing of lenalidomide as follows: First occasion: resume at 15mg daily dose Second occasion: resume at 10mg daily dose Third occasion: resume at 5mg daily dose

*also consider omitting some cyclophosphamide doses from future cycles, if included

Renal Impairment:

CrCl (ml/min)	Lenalidomide Dose
30 - 49	10mg once daily#
< 30 (not requiring dialysis)	15mg every other day##
< 30 (requiring dialysis)	5mg once daily (taken after dialysis on dialysis days)

May be escalated to 15 mg once daily after 2 cycles if patient is not responding to treatment and is tolerating the treatment.
May be escalated to 10 mg once daily if the patient is tolerating the treatment.

CrCl (ml/min)	Cyclophosphamide Dose
> 20	Give 100% dose
10 – 20	Give 75% dose
< 10	Give 50% dose

Hepatic Impairment: Lenalidomide has not formally been studied in patients with impaired hepatic function and there are no specific dose recommendations.
Consider the possibility of lenalidomide-induced liver injury in patients with unexplained deterioration of liver function. If associated, liver function generally recovers when lenalidomide is stopped.

Steroid Side Effects: If severe steroid-related side effects develop, dose reduction to dexamethasone 20mg per dose may be considered.

Patient Information: Macmillan leaflet for Lenalidomide, and Cyclophosphamide if included
Patient Booklet "Treatment with Revlimid for Multiple Myeloma"
Revlimid Infoguide produced by Myeloma UK (available at www.myelomaonline.org.uk) is also recommended

References:
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