Lenalidomide & Dexamethasone for Multiple Myeloma

NHS England

Cumbria, Northumberland, Tyne & Wear Area Team

DRUG ADMINISTRATION SCHEDULE

First 4 cycles

Day	Drug	Dose	Route	Frequency	
1 to 21	Lenalidomide	25mg	Oral	Once daily	**21 days only**
1 to 4, 9 to12, 17 to 20	Dexamethasone	40mg (see administration notes below)	Oral	Once daily	**On specified days only**

Cycle 5 onwards

Day	Drug	Dose	Route	Frequency	
1 to 21	Lenalidomide	25mg	Oral	Once daily	**21 days only**
1 to 4 only	Dexamethasone	40mg (see administration notes below)	Oral	Once daily	**4 days only**

CYCLE LENGTH AND NUMBER OF DAYS

28 Day cycle, given until disease progression.

APPROVED INDICATIONS

Patients with Multiple Myeloma who have received two or more prior therapies, provided the drug cost of lenalidomide for patients who remain on treatment for more than 26 cycles will be met by the manufacturer.

Approved for use on the National Cancer Drugs Fund List for treatment of patients with multiple myeloma who meet the following criteria:

1. Application made by and first cycle of systemic anti-cancer therapy to be prescribed by a consultant specialist specifically trained and accredited in the use of systemic anti-cancer therapy

2. Multiple myeloma

3. 2nd line indication

4. a. Contra-indication to the use of Bortezomib OR

   b. Previously received Bortezomib in the first line setting

ELIGIBILITY CRITERIA

Patients who have received two or more prior therapies for multiple myeloma. Absolute Neutrophil Counts (ANC) ≥ 1.0 x 10^9/l, Platelet counts ≥ 75 x 10^9/l (or dependent on bone marrow infiltration by plasma cells platelet counts ≥ 30 x 10^9/l.)

EXCLUSION CRITERIA

Pregnancy / Breast Feeding

For women of childbearing potential, lenalidomide is contraindicated unless all of the following are met:

- She understands the expected teratogenic risk to the unborn child.

- She understands the need for effective contraception, without interruption, 4 weeks before starting treatment, throughout the entire duration of treatment, and 4 weeks after the end of treatment
- Even if a woman of childbearing potential has amenorrhea she must follow all the advice on effective contraception
- She should be capable of complying with effective contraceptive measures
- She is informed and understands the potential consequences of pregnancy and the need to rapidly consult if there is a risk of pregnancy
- She understands the need to commence the treatment as soon as lenalidomide is dispensed following a negative pregnancy test
- She understands the need and accepts to undergo pregnancy testing every 4 weeks except in case of confirmed tubal sterilisation
- She acknowledges that she understands the hazards and necessary precautions associated with the use of lenalidomide.

RECOMMENDED TAKE HOME MEDICATION

Gastro-protection will usually be required with high dose dexamethasone (e.g. Omeprazole 20mg once daily)

Patients with high tumour burden at the start of treatment may require allopurinol.

Thrombo-prophylaxis using standard medical prophylaxis dose of Low Molecular Weight Heparin (LMWH) should be prescribed (unless contra-indicated) with all thalidomide-chemotherapy combinations. Duration of LMWH remains uncertain but should be at least for the first 3 months of treatment when the risk of VTE is greatest. LMWH requires dose reduction in renal impairment.

INVESTIGATIONS / MONITORING REQUIRED

Prior to first cycle: FBC, U&Es, LFTs, Calcium, Paraprotein

Prior to each cycle: FBC, U&Es, LFTs, Calcium, Paraprotein

Patients should have a weekly FBC checked during the first 8 weeks of therapy and treatment interrupted if FBC is outside of the limits listed on page 3.

ASSESSMENT OF RESPONSE

Paraprotein

REVIEW BY CLINICIAN

Prior to each cycle (unless being seen by a nurse / pharmacist – see below)

NURSE / PHARMACIST LED REVIEW

Nurse or pharmacist led review, within a locally agreed protocol, is acceptable on day 1 for all cycles except the first, and middle cycle. If nurse or pharmacist is reviewing the patient they must comply with the necessary precautions of the Pregnancy Prevention Programme

ADMINISTRATION NOTES

- Capsules are available in 5mg, 10mg, 15mg and 25mg strengths. The price structure of lenalidomide means that multiple capsules should never be used to make up a dose.

Lenalidomide & Dexamethasone for Multiple Myeloma

- Revlimid capsules should be taken at about the same time each day. The capsules should not be broken or chewed. The capsules should be swallowed whole, preferably with water, either with or without food.
- If less than 12 hours has elapsed since missing a dose, the patient can take the dose. If more than 12 hours has elapsed since missing a dose at the normal time, the patient should not take the dose, but take the next dose at the normal time on the following day

- Revlimid (Lenalidomide) has the potential to be teratogenic (it is structurally related to thalidomide). **Celgene operates a pregnancy prevention programme to prevent potential harm. Refer to the Celgene documentation prior to prescribing and dispensing.**
- Dispensing pharmacy must be registered to supply.
- A prescription authorisation form (dated the same as the prescription) must accompany the prescription to pharmacy.
- Patients should be instructed never to give this medicinal product to another person and to return any unused capsules to their pharmacist at the end of treatment.
- Patients should not donate blood or semen during therapy or for 1 week following discontinuation of lenalidomide.
- Dexamethasone Dose: Recent evidence (Rajkumar 2009) has shown that *short term* survival is reduced in patients receiving high dose dexamethasone. Clinicians are encouraged to consider this evidence when prescribing.

TOXICITIES

Common: Myelosuppression – Neutropenia & Thrombocytopenia, Fatigue, Thrombosis, Neuropathy, Constiipation, Muscle Cramps, Anaemia, Rash, Increased rate of Infections (bacterial, viral and fungal) .Alopecia,
Less Common: Altered thyroid function.

DOSE MODIFICATION / TREATMENT DELAYS

The cost of lenalidomide capsules is not proportional to the amount of drug in the capsule. Please try to use the dose modifications listed below. (Giving 20mg 75% more than giving 25mg).

Starting dose	25mg Daily (21 days)
Level 1	15mg Daily (21 days)
Level 2	10mg Daily (21 days)
Level 3	5mg Daily (21 days)

Haematological Toxicity:

(Note: where haematological disease is affecting bone marrow function, lower treatment parameters may be acceptable. This should be clearly documented for the specific patient.)

Delay treatment on Day 1 if ANC < 1.0 x 10^9cells/l or PLT < 75 x 10^9cells/l (or 30 10^9cells/l if marrow infiltration

If PLT during treatment fall < 30 x 10^9cells/l interrupt treatment until ≥ 30 x 10^9cells/l.

Treatment can then be restarted at the next dose level (i.e. Level 1). If PLT drop for a second time < 30 x 10^9cells/l interrupt treatment and restart at the next lowest dose (i.e. Level 2). (Do not give doses lower than 5mg daily)

If ANC during treatment fall < 0.5 x 10^9cells/l interrupt treatment until ≥ 0.5 x 10^9cells/l. Treatment can then be restarted at the original dose level (unless other toxicities observed). If ANC drop for a second time < 0.5 x 10^9cells/l interrupt treatment and restart at the next lowest dose (i.e. Level 1). (Do not give doses lower than 5mg daily)

Renal Function:
Lenalidomide is renally excreted. Dose modification is necessary:

CrCl	Lenalidomide Dose
≥ 50 ml/min	25mg Daily (21days)
30 – 49.9ml/min	10mg daily (21days) increase to 15mg after 2 cycles if tolerated
< 30ml/min, not on dialysis	15mg alternate days (total 21 days – i.e. 11 capsules)
< 30ml/min, needing dialysis	5mg daily (on dialysis days after dialysis)

TREATMENT LOCATION
Suitable for self administration in patients own homes, under the supervision of haematology teams from Level 1 – 4 Haematology Services.

REFERENCES:

Summary of Product Characteristics, Celgene. March 2009
Vincent Rajkumar *et al***.** Lenalidomide plus high-dose dexamethasone versus lenalidomide plus low-dose dexamethasone as initial therapy for newly diagnosed multiple myeloma: an open-label randomised controlled trial**.** Lancet Oncology, Early Online Publication, 22 October 2009

Document Control

Document Title:	Lenalidomide NECN protocol CRP09 H040		
Document No:	CRP09 H040	**Current Version:**	3.2
Author:	Calum Polwart, Network Pharmacist NECN	**Reviewed by:**	Calum Polwart
Approved by:	Anne Lennard / Diane Plews	**Date Reviewed:**	28 May 2014
Due for Review:	June 2016		
Summary of Changes	1.0a	Initial version agreed	
	2.0a	Weekly bloods for 8 weeks added	
	3.0a	Added LMWH Guidance. Reference to reduced dose dexamethasone added. Document number changed.	
	3.1	Protocol reviewed. Typing errors corrected.	
	3.2	Protocol reviewed. Typing errors corrected.	