**Chemotherapy Protocol**

# MULTIPLE MYELOMA

## LENALIDOMIDE

### Regimen

- Multiple Myeloma – Lenalidomide

### Indication

- Lenalidomide is recommended, within its licensed indication, as an option for the treatment of multiple myeloma only in people who have received two or more prior therapies.

### Toxicity

| Drug | Adverse Effect |
|---|---|
| Lenalidomide | Peripheral neuropathy, bone marrow suppression, pneumonia, infections, venous thrombotic events, respiratory dysfunction, rashes, hypokalaemia, hypomagnesaemia, hypocalcaemia, teratogenic risk, GI disturbances, flu-like symptoms. |

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

### Monitoring

*Drugs*

- FBC, LFTs and U&Es prior to day one of treatment
- Calcium and magnesium levels at regular intervals throughout treatment
- Thyroid function tests at baseline and at regular intervals throughout treatment
- Perform a venous thromboembolism (VTE) risk assessment prior to starting treatment.
- Pregnancy prevention programme for lenalidomide

### Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

*Haematological*

Dose modifications for haematological toxicity in the table below are for general guidance only. Always refer to the responsible consultant as any dose reductions or delays will be dependent on clinical circumstances and treatment intent. Low counts can be a consequence of bone marrow infiltration as well as drug toxicity.

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL (80g/L).

| **Neutrophils ($x10^9$/L)** | **Dose Modifications** |
|---|---|
| 1 or more | 100% |
| Less than 1 | 1st Occurrence<br>Delay until recovery has occurred. Restart at full dose.<br>2nd Occurrence<br>Delay until recovery has occurred. Restart at a dose of 15mg<br>3rd Occurrence<br>Delay until recovery has occurred. Restart at a dose of 10mg<br>3rd Occurrence<br>Delay until recovery has occurred. Restart at a dose of 5mg |
| **Platelets ($x10^9$/L)** | **Dose Modifications** |
| 50 or more | 100% |
| Less than 50 | 1st Occurrence<br>Delay until recovery has occurred. Restart at a dose of 15mg<br>2nd Occurrence<br>Delay until recovery has occurred. Restart at a dose of 10mg<br>3rd Occurrence<br>Delay until recovery has occurred. Restart at a dose of 5mg |

*Hepatic Impairment*

| **Drug** | **Bilirubin µmol/L** | | **AST/ALT units/L** | **Dose (% of original dose)** |
|---|---|---|---|---|
| Lenalidomide | | | | No dose adjustments needed |

*Renal Impairment*

| Drug | Creatinine Clearance (ml/min) | Dose (% of original dose) |
|---|---|---|
| Lenalidomide | Greater than 50 | 100% |
| | 30-50 | Start treatment with 10mg once a day |
| | Less than 30 | Start treatment with 15mg on alternate days |
| | Less than 30 and requiring dialysis | 5 mg once a day<br>On dialysis days, the dose should be administered following dialysis. |

*Other*

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

In general for all other non-haematological NCI-CTC grade 3 and above toxicities delay treatment until the adverse effect has resolved to NCI-CTC grade 1 or below. Reduce the daily dose to 15mg. On subsequent occurrences delay until recovery the dose may then be reduced to 10mg and 5mg consecutively. If a dose of 5mg is not tolerated treatment should be stopped.

Allergic or hypersensitivity reactions that occur at NCI-CTC grade 2, withhold treatment until the symptoms have resolved to NCI-CTC grade 1 or below. Treatment may be cautiously restarted at a daily dose of 15mg. For NCI-CTC grade 3 or above reactions discontinue the lenalidomide.

Lenalidomide should be discontinued if a desquamating rash of NCI-CTC grade 3 or above or NCI-CTC grade 4 non-desquamating rash develops.

There is an increased risk of thrombosis and some form of prophylaxis is recommended. A low molecular weight heparin or warfarin should be prescribed initially. If patients are treated with either a low molecular weight heparin or warfarin consider switching patients to aspirin after six cycles of therapy or after maximum response is achieved. A high index of suspicion for venous thromboembolism should be maintained. If a venous thrombosis or embolism NCI-CTC grade 3 or above then stop treatment and start anticoagulation. Lenalidomide may be reinstated at the clinician's discretion, if the patient is fully anti-coagulated.

## Regimen

**28 day cycle until disease progression or intolerance (12 cycles will be set in ARIA)**

| Drug | Dose | Days | Administration |
|---|---|---|---|
| Lenalidomide | 25mg | 1-21 incl. | Oral |

## Dose Information

- Lenalidomide is available as 25mg, 15mg, 10mg, 7.5mg, 5mg and 2.5mg capsules

## Administration Information

- Lenalidomide should be swallowed whole, preferably with water, either with or without food at about the same time each day. The capsules should not be opened, broken or chewed. 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

## Additional Therapy

- Antiemetics
    - metoclopramide 10mg three times a day when required oral
- Consider allopurinol 300mg once a day for 7 days in cycle 1 only
- Thromboprophylaxis a low molecular weight heparin according to local formulary choice. Aspirin may be considered after six cycles or when maximal response is achieved.

## Additional Information

- Patient, prescriber and pharmacy must comply with the pregnancy prevention programme.
- The National Patient Safety Agency alert NPSA/2008/RRR001 must be followed when prescribing, dispensing or administering oral chemotherapy.
- It must be made clear to all staff, including those in the community, that this is a short course of oral chemotherapy that must not be continued.
- Patients should be assessed for suitability for oral chemotherapy prior to starting treatment.

## Coding

- Procurement – X71.5
- Delivery – X73.1

References
1. Weber DM et al. Lenalidomide plus Dexamethasone for Relapsed Multiple Myeloma in North America. N Eng J Med 2007; 357: 2133-42
2. Dimopoulos Met al. Lenalidomide plus Dexamethasone for Relapsed or Refractory Multiple Myeloma. N Eng J Med 2007; 357: 2123-32

## REGIMEN SUMMARY

Lenalidomide

### Cycle One Day One

### Take Home Medicines

1. Warning – Pregnancy Prevention Programme
   Administration Instructions
   Lenalidomide is associated with a pregnancy prevention programme. Please ensure this is completed for all patients.

2. Lenalidomide 25mg once a day for 21 days oral
   Administration Instructions
   Lenalidomide is associated with a pregnancy prevention programme. Please ensure this is completed for all patients.

   Oral chemotherapy.

   Available as 25mg, 15mg, 10mg, 7.5mg, 5mg and 2.5mg capsules, please ensure dose modifications occur in multiples of these strengths.

   Swallow whole, not chewed with plenty of water.

3. Metoclopramide 10mg three times a day when required oral*
   Administration Instructions
   When required for the relief of nausea. Please supply 28 tablets or nearest original pack size

4. Allopurinol 300mg once a day for 7 days only oral
   Administration Instructions
   Take with or after food with plenty of water. Please supply 7 days.

5. Thromboprophylaxis according to local formulary choice;
   Administration Instructions
   The choice of thromboprophylaxis is dependent on local formularly choice and may include;

   - dalteparin 5000units once a day subcutaneous injection
   - enoxaparin 40mg once a day subcutaneous injection
   - heparin 5000units twice a day subcutaneous injection

   Please supply 28 days or nearest original pack size. Aspirin may be considered after cycle six of treatment.

### Cycle Two Onwards

### Take Home Medicines

6. Warning – Pregnancy Prevention Programme
   Administration Instructions
   Lenalidomide is associated with a pregnancy prevention programme. Please ensure this is completed for all patients.

7. Lenalidomide 25mg once a day for 21 days oral
   Administration Instructions
   Lenalidomide is associated with a pregnancy prevention programme. Please ensure this is completed for all patients.

   Oral chemotherapy.

   Available as 25mg, 15mg, 10mg, 7.5mg, 5mg and 2.5mg capsules, please ensure dose modifications occur in multiples of these strengths.

   Swallow whole, not chewed with plenty of water.

8. Thromboprophylaxis according to local formulary choice;

Administration Instructions

The choice of thromboprophylaxis is dependent on local formularly choice and may include;

- dalteparin 5000units once a day subcutaneous injection
- enoxaparin 40mg once a day subcutaneous injection
- heparin 5000units twice a day subcutaneous injection

Please supply 28 days or nearest original pack size. Aspirin may be considered after cycle six of treatment.

*The metoclopramide will be supplied on cycle one only. Thereafter it can be added from supportive treatments if further supplies are required.

## DOCUMENT CONTROL

| Version | Date | Amendment | Written By | Approved By |
|---|---|---|---|---|
| 1 | April 2018 | None | Dr Deborah Wright Pharmacist | Dr S Narayanan Consultant Haematologist |

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury Hospitals NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors that occur as a result of following these guidelines. These are guidelines only and should not be relied upon as the only source of information. They should be read in conjunction with the Summary of Product Characteristics (www.medicines.org.uk) and latest research papers.