

## Chemotherapy Protocol

### MULTIPLE MYELOMA

#### MPV (IV)-BORTEZOMIB (IV)-MELPHALAN (PO)-PREDNISOLONE (35 day)

##### Regimen

- Multiple Myeloma – MPV(IV)-Bortezomib (IV)-Melphalan (PO)-Prednisolone (35 day)

##### Indication

- The treatment of relapsed or refractory multiple myeloma

##### Toxicity

Drug	Adverse Effect
Bortezomib	GI disturbances, peripheral neuropathy, hypotension, dizziness, blurred vision, headache, musculoskeletal pain, pyrexia
Melphalan	Gastro-intestinal disturbances, stomatitis, nausea, vomiting, alopecia, myalgia, muscle atrophy and fibrosis
Prednisolone	Weight gain, GI disturbances, hyperglycaemia, CNS disturbances, cushingoid changes, glucose intolerance

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

##### Monitoring

- FBC, LFTs and U&Es prior to day 1 of each cycle. FBC on days 8, 15, and 22 are optional
- Paraprotein or light chains every 5 weeks
- Regular monitoring of blood glucose is considered good practice but optional

##### 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 or erythropoietin if the patient is symptomatic of anaemia or has a haemoglobin of less than 8g/dL.

Dose modifications based on haematological parameters apply to melphalan only.

Neutrophils (x10 <sup>9</sup> /L)	Dose Modifications (bortezomib, melphalan)
1 or greater	100%
less than 1	Delay treatment for up to 2 weeks until the neutrophils are 1x10 <sup>9</sup> /L or above and then continue with full dose and growth factor support and/or dose reduction. If recovery takes longer than 2 weeks consider stopping treatment.
Platelets (x10 <sup>9</sup> /L)	Dose Modifications (melphalan)
75 or above	100%
less than 75	Delay treatment for up to 2 weeks until the platelets are 75x10 <sup>9</sup> /L or above and then continue with reduced dose. If recovery takes longer than 2 weeks consider stopping treatment.

### Hepatic Impairment

Please note that the approach may be different where abnormal liver function tests are due to disease involvement.

Drug	Bilirubin $\mu$ mol/L	AST/ALT units/L	Dose (% of original dose)
Melphalan	N/A	N/A	No dose adjustment necessary
Bortezomib	1.5xULN or below	N/A	100%
	greater than 1.5xULN	N/A	Initiate treatment at 0.7mg/m <sup>2</sup> . The dose may be escalated to 1mg/m <sup>2</sup> or reduced to 0.5mg/m <sup>2</sup> in subsequent cycles based on patient tolerability.

### Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Melphalan	30 or greater	100%
	less than 30	Initiate treatment at 75% increase at subsequent cycles if tolerated
Bortezomib	greater than 20	100%
	20 and below	Clinical decision

## 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.

## Bortezomib

### Neuropathic pain and/or peripheral neuropathy

For patients experiencing NCI-CTC grade 1 neuropathy continue with full dose.

For NCI-CTC grade 1 with pain or grade 2 neuropathy reduce the dose of bortezomib to  $1\text{mg}/\text{m}^2$  or switch to a weekly bortezomib at the standard dose of  $1.3\text{mg}/\text{m}^2$

For NCI-CTC grade 2 with pain or grade 3 neuropathy discontinue treatment until symptoms have resolved to NCI-CTC grade 1 or less then reinitiate bortezomib at a dose of  $0.7\text{mg}/\text{m}^2$

For NCI-CTC grade 4 neuropathy and/or severe autonomic neuropathy discontinue bortezomib.

Subcutaneous administration should also be considered as the incidence and severity of peripheral neuropathy has been shown to be less when bortezomib is given by this route.

For any other NCI-CTC grade 3 non haematological toxicity bortezomib should be discontinued until symptoms have resolved to NCI-CTC grade 1 or below. On the first occurrence treatment may be reinitiated at a dose of  $1\text{mg}/\text{m}^2$ . Following second occurrence to dose should be further reduced to  $0.7\text{mg}/\text{m}^2$  once symptoms have resolved.

If the toxicity is not resolved or if it recurs at the lowest dose, discontinuation of bortezomib must be considered unless the benefit of treatment clearly outweighs the risk.

## Prednisolone

For patients who are elderly or unable to tolerate the standard dose of prednisolone the dose may be reduced or omitted as appropriate.

## Regimen

### 35 day cycle for 8 cycles

Drug	Dose	Days	Administration
Bortezomib	$1.3\text{mg}/\text{m}^2$	1, 8, 15, 22	Intravenous injection over 5 seconds
Melphalan	$7\text{mg}/\text{m}^2$	1,2,3,4	Oral
Prednisolone	$60\text{mg}/\text{m}^2$	1,2,3,4	Oral

Response to treatment should be assessed each cycle. Continue to a maximum of eight treatment cycles if there is at least a partial response, defined as a 50% reduction in paraprotein after four cycles.

Prednisolone may be omitted or the dose reduced at the clinician's discretion.

### Dose Information

- Bortezomib will be dose rounded to the agreed bands
- Melphalan dose will be rounded to the nearest 2mg (up if halfway)
- Melphalan is available as 2mg tablets
- Prednisolone dose will be rounded to the nearest 5mg (up if halfway)
- Prednisolone is available as 5mg, 20mg and 25mg tablets

### Administration Information

- Melphalan tablets should be stored in the fridge
- Prednisolone should be taken in the morning, with or after food

### Additional Therapy

- Anti-emetics

As take home medication

- metoclopramide 10mg three times a day oral when required
- Consider allopurinol 300mg once a day for seven days for cycle one only
- Anti-infective prophylaxis with
  - aciclovir 400mg twice a day oral
  - co-trimoxazole 960mg once day on Monday, Wednesday and Friday oral
- Bisphosphonates in accordance with local policies
- Mouthwashes according to local or national policy on the treatment of mucositis.
- Gastric protection with a proton pump inhibitor or a H<sub>2</sub> antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

### Additional Information

- 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 – X72.3, X72.4

### References

1. San Miguel JF, Schlag R, Khuageva NK et al. Bortezomib plus melphalan and prednisolone for multiple myeloma. N Engl J Med 2008; 359: 2613-2614.

## REGIMEN SUMMARY

MPV (IV)-Bortezomib (IV)-Melphalan (PO)-Prednisolone (35 day)

### Cycle 1

#### Day 1, 8, 15, 22

1. Bortezomib 1.3mg/m<sup>2</sup> intravenous injection over 5 seconds

#### Take Home Medicines (day 1 only)

2. Melphalan 7mg/m<sup>2</sup> once a day on days 1, 2, 3, 4 days oral  
Administration Instructions  
Tablets should be stored in the refrigerator. Oral chemotherapy.
3. Prednisolone 60mg/m<sup>2</sup> once a day on days 1, 2, 3, 4 days oral  
Administration Instructions  
Take in the morning, with or after food.
4. Metoclopramide 10mg up to three times a day when required oral  
Administration Instructions  
When required for the relief of nausea. Please dispense 28 tablets or nearest original pack size.
5. Aciclovir 400mg twice a day for 35 days oral  
Administration Instructions  
Please supply 35 tablets or an original pack if appropriate.
6. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday for 35 days oral  
Administration Instructions  
Co-trimoxazole 960mg once a day on Mondays, Wednesdays and Fridays. Please supply 35 days.  
This may be dispensed as 480mg twice a day on Mondays, Wednesdays and Fridays according to local practice.
7. Allopurinol 300mg once a day for 7 days oral  
Administration Instructions  
Take with or after food with plenty of water. Please supply 7 days.
8. Gastric Protection  
Administration Instructions  
The choice of gastric protection is dependent on local formulary choice and may include;
  - esomeprazole 20mg once a day oral
  - omeprazole 20mg once a day oral
  - lansoprazole 15mg once a day oral
  - pantoprazole 20mg once a day oral
  - rabeprazole 20mg once a day oral
  - cimetidine 400mg twice a day oral
  - famotidine 20mg once a day oral
  - nizatidine 150mg twice a day oral
  - ranitidine 150mg twice a day oral

Please supply 35 days or nearest original pack size.

### Cycle 2 onwards

#### Day 1, 8, 15, 22

9. Bortezomib 1.3mg/m<sup>2</sup> intravenous injection over 5 seconds

## Take Home Medicines (day 1 only)

### 10. Melphalan 7mg/m<sup>2</sup> once a day on days 1, 2, 3, 4 days oral

#### Administration Instructions

Tablets should be stored in the refrigerator. Oral chemotherapy.

### 11. Prednisolone 60mg/m<sup>2</sup> once a day on days 1, 2, 3, 4 days oral

#### Administration Instructions

Take in the morning, with or after food.

### 12. Metoclopramide 10mg up to three times a day when required oral

#### Administration Instructions

When required for the relief of nausea. Please dispense 28 tablets or nearest original pack size.

### 13. Aciclovir 400mg twice a day for 35 days oral

#### Administration Instructions

Please supply 35 tablets or an original pack if appropriate.

### 14. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday for 35 days oral

#### Administration Instructions

Co-trimoxazole 960mg once a day on Mondays, Wednesdays and Fridays. Please supply 35 days.

This may be dispensed as 480mg twice a day on Mondays, Wednesdays and Fridays according to local practice.

### 15. Gastric Protection

#### Administration Instructions

The choice of gastric protection is dependent on local formulary choice and may include;

- esomeprazole 20mg once a day oral
- omeprazole 20mg once a day oral
- lansoprazole 15mg once a day oral
- pantoprazole 20mg once a day oral
- rabeprazole 20mg once a day oral
- cimetidine 400mg twice a day oral
- famotidine 20mg once a day oral
- nizatidine 150mg twice a day oral
- ranitidine 150mg twice a day oral

Please supply 35 days or nearest original pack size.

## DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	May 2016	None	Rebecca Wills Pharmacist  Dr Deborah Wright Pharmacist	Dr Mathew Jenner 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 Hospital 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.