Myeloma-Carfilzomib-Dexamethasone (20)  

Chemotherapy Protocol  

**MYELOMA**  

**Carfilzomib-Dexamethasone (20)**  

**Regimen**  

- Myeloma – Carfilzomib-Dexamethasone (20)  

**Indication**  

- Carfilzomib in combination with dexamethasone is an option for treating multiple myeloma in adults if the patient has had one previous therapy which did not include bortezomib.  
- Treatment intent – disease modification  
- WHO performance status 0, 1, 2  

**Toxicity**  

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adverse Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carfilzomib</td>
<td>Anaemia, fatigue, diarrhoea, thrombocytopenia, nausea, pyrexia, dyspnoea, respiratory tract infection, cough and peripheral oedema, confusional states, herpes zoster infection</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>Weight gain, gastrointestinal disturbances, hyperglycaemia, CNS disturbances, cushingoid changes, glucose intolerance.</td>
</tr>
</tbody>
</table>

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

**Monitoring**  

- FBC, LFT and U&Es prior to day 1 of treatment  
- Regular monitoring of blood glucose is considered good practice.
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).

Prior to starting a new cycle of treatment;

- neutrophils should be greater than or equal to 1x10⁹/L
- platelets should be greater than or equal to 50x10⁹/L
- non-haematological toxicity should resolve to NCI-CTC grade 1 or below or baseline

<table>
<thead>
<tr>
<th>Haematological dose modifications – Carfilzomib</th>
</tr>
</thead>
<tbody>
<tr>
<td>This table refers to toxicity during a cycle of treatment (nadir / mid cycle)</td>
</tr>
</tbody>
</table>

### Neutrophils

| Dose | 
|---|---|
| Greater than or equal to 0.5x10⁹/L | 100% |
| Less than 0.5x10⁹/L | Withhold dose until neutrophils recover to 0.5x10⁹/L or above |
| | 1st occurrence: After neutrophil recovery restart at current dose level |
| | 2nd occurrence: After neutrophil recovery restart and consider 1 dose level reduction (see table below) |

### Platelets

| Dose | 
|---|---|
| Greater than 10x10⁹/L | 100% |
| Less than 10x10⁹/L | Withhold dose until the platelets are 10x10⁹/L or above |
| | 1st occurrence: After platelet recovery and / or bleeding controlled, continue at current dose level |
| | 2nd occurrence: After platelet recovery and / or bleeding controlled, restart carfilzomib and consider 1 dose level reduction (see table below) |
**Hepatic impairment**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carfilzomib</td>
<td>No information available</td>
</tr>
</tbody>
</table>

**Renal Impairment**

<table>
<thead>
<tr>
<th>Renal function</th>
<th>Dose (% of original dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine greater than or equal to 2x baseline, and / or</td>
<td>• Withhold dose</td>
</tr>
<tr>
<td>CrCl less than 15ml/min, and / or</td>
<td>• Restart carfilzomib when renal function has recovered to within 25% of baseline (consider 1 dose level reduction) – see table below.</td>
</tr>
<tr>
<td>CrCl decreased to less than or equal to 50% of baseline</td>
<td></td>
</tr>
</tbody>
</table>

**Other**

<table>
<thead>
<tr>
<th>Other non-haematological toxicity</th>
<th>Recommended action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 3 or 4 toxicity</td>
<td>• Stop until toxicity resolved / returned to baseline</td>
</tr>
<tr>
<td></td>
<td>• Consider restarting at 1 dose level reduction</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Carfilzomib dose level reductions:*</th>
<th>Normal dose</th>
<th>1st reduction</th>
<th>2nd reduction</th>
<th>3rd reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>56mg/m²</td>
<td>45mg/m²</td>
<td>36mg/m²</td>
<td>27mg/m²</td>
</tr>
</tbody>
</table>

*Note: carfilzomib dose and dose reductions differ depending on regimen used.

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.

For all other non-haematological NCI-CTC toxicities refer to manufacturer information.

**Carfilzomib**

**Infusion reactions**

Infusion reactions, including life-threatening reactions, have been reported in patients who received carfilzomib. Symptoms may include fever, chills, arthralgia, myalgia, facial flushing, facial oedema, vomiting, weakness, shortness of breath, hypotension, syncope, chest tightness, or angina. These reactions can occur immediately following or up to 24 hours after
administration of carfilzomib. Dexamethasone should be administered prior to carfilzomib to reduce the incidence and severity of reactions.

Monitor for signs and symptoms of an infusion-related reaction. Interrupt or slow the rate of infusion in patients with mild or moderate infusion reactions and consider pre-medications prior to subsequent doses.

**Dexamethasone**

<table>
<thead>
<tr>
<th>Dose Level</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 (starting)</td>
<td>20mg</td>
</tr>
<tr>
<td>1</td>
<td>10mg</td>
</tr>
</tbody>
</table>

If recovery from toxicities is prolonged beyond 14 days, then the dose of dexamethasone will be decreased by one dose level.

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Grade (NCI-CTC)</th>
<th>Dose modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspepsia</td>
<td>1 - 2</td>
<td>Maintain dose and treat with histamine (H₂) antagonist or proton pump inhibitor. Decrease by one dose level if symptoms persist.</td>
</tr>
<tr>
<td></td>
<td>3 or above</td>
<td>Interrupt dose until symptoms are controlled. Add H₂ blocker or proton pump inhibitor and decrease one dose level when dose restarted.</td>
</tr>
<tr>
<td>Oedema</td>
<td>3 or above</td>
<td>Use diuretics as needed and decrease dose by one dose level.</td>
</tr>
<tr>
<td>Confusion or mood alteration</td>
<td>2 or above</td>
<td>Interrupt dose until symptoms resolve. When dose restarted decrease dose by one dose level.</td>
</tr>
<tr>
<td>Muscle weakness</td>
<td>2 or above</td>
<td>Interrupt dose until the muscle weakness is grade 1 or below. Restart with dose decreased by one level.</td>
</tr>
<tr>
<td>Hyperglycaemia</td>
<td>3 or above</td>
<td>Decrease dose by one dose level. Treat with insulin or oral hypoglycaemic agents as needed</td>
</tr>
<tr>
<td>Acute pancreatitis</td>
<td></td>
<td>Discontinue patient from dexamethasone treatment regimen.</td>
</tr>
<tr>
<td>Other</td>
<td>3 or above</td>
<td>Stop dexamethasone dosing until adverse event resolves to grade 2 or below. Resume with dose reduced by one level.</td>
</tr>
</tbody>
</table>

**Regimen**

Warning, the day one dexamethasone is incorporated into the regimen as a dose to be administered prior to the carfilzomib by the nursing staff. If the day one carfilzomib is suspended for any reason the schedule of the dexamethasone may need to be adjusted and the administration instructions amended.
28 day cycle until disease progression or intolerance occurs (12 cycles will be set in ARIA)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Days</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carfilzomib (cycle 1)</td>
<td>20mg/m² (max 44mg)</td>
<td>1, 2</td>
<td>IV infusion in 100ml glucose 5% over 30 minutes</td>
</tr>
<tr>
<td>Carfilzomib (cycle 1)</td>
<td>56mg/m² (max 123mg)</td>
<td>8, 9, 15, 16</td>
<td></td>
</tr>
<tr>
<td>Carfilzomib (cycles 2 onwards)</td>
<td>56mg/m² (max 123mg)</td>
<td>1, 2, 8, 9, 15, 16</td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>20mg</td>
<td>1, 2, 8, 9, 15, 16, 22, 23</td>
<td>Oral</td>
</tr>
</tbody>
</table>

**Dose Information**

- Carfilzomib will be dose banded in accordance with the nationally agreed dose bands (2mg/ml)
- Carfilzomib will be dose capped at 2.2m²
- Dexamethasone is available as 500microgram, 2mg and 4mg tablets and as a 2mg/5ml oral liquid.

**Administration Information**

- Dexamethasone should be taken in the morning, with or after food

**Extravasation**

- Carfilzomib - neutral

**Additional Therapy**

- No antiemetics are required.
- Carfilzomib pre-hydration with sodium chloride 0.9% 500ml over 30 minutes
- Carfilzomib post hydration with sodium chloride 0.9% 500ml over 30 minutes
- For the treatment of carfilzomib related Infusion reactions
  - chlorphenamine 10mg intravenous injection once only when required for infusion related reactions
  - hydrocortisone 100mg intravenous when required for infusion related reactions
  - salbutamol 2.5mg nebule when required for related bronchospasm
  - paracetamol 1000mg oral once only when required for infusion related reactions
- Consider allopurinol 300mg oral once a day for seven days for the first cycle only
• Consider anti-infective prophylaxis including;
  - aciclovir 400mg twice a day oral
  - co-trimoxazole 960mg once a day oral on Monday, Wednesday and Friday only
  - fluconazole 50mg once a day 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 H₂ antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

Coding

• Procurement – X71.3

• Delivery – X72.2

References
REGIMEN SUMMARY
Carfilzomib-Dexamethasone (20)

Cycle 1, Day 1, 2

1. Dexamethasone 20mg oral 30 minutes prior to the carfilzomib
   Administration Instructions
   Administer at least 30 minutes and up to four hours prior to the start of the carfilzomib infusion

2. Sodium chloride 0.9% 500ml intravenous infusion over 30 minutes

3. Carfilzomib 20mg/m² (maximum 44mg) intravenous infusion in 100ml glucose 5% over 30 minutes

4. Sodium chloride 0.9% 500ml intravenous infusion over 30 minutes

5. Chlorphenamine 10mg intravenous injection once only when required for infusion related reactions.

6. Hydrocortisone 100mg intravenous injection once only when required for infusion related reactions

7. Salbutamol 2.5mg nebule once only when required for infusion related bronchospasm

8. Paracetamol 1000mg oral once only when required for infusion related reactions
   Administration Instructions
   Please check if the patient has taken paracetamol. Maximum dose is 4g per 24 hours. There should be 4 hours between doses

Cycle 1, Day 8, 9, 15, 16

9. Dexamethasone 20mg oral 30 minutes prior to the carfilzomib
   Administration Instructions
   Administer at least 30 minutes and up to four hours prior to the start of the carfilzomib infusion

10. Sodium chloride 0.9% 500ml intravenous infusion over 30 minutes

11. Carfilzomib 56mg/m² (maximum 123 mg) intravenous infusion in 100ml glucose 5% over 30 minutes

12. Sodium chloride 0.9% 500ml intravenous infusion over 30 minutes

13. Chlorphenamine 10mg intravenous injection once only when required for infusion related reactions.

14. Hydrocortisone 100mg intravenous injection once only when required for infusion related reactions

15. Salbutamol 2.5mg nebule once only when required for infusion related bronchospasm

16. Paracetamol 1000mg oral once only when required for infusion related reactions
   Administration Instructions
   Please check if the patient has taken paracetamol. Maximum dose is 4g per 24 hours. There should be 4 hours between doses
Take home medicines (Cycle 1 Day 1 only)

17. Dexamethasone 20mg once a day on day 22, 23 oral
   Administration Information
   Please supply two doses of dexamethasone on day 1 of the cycle, ONE dose to be taken on day 22 and on day 23 of the cycle once a day in the morning.
   Take with or after food.

18. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday for 28 days oral
   Administration Information
   Co-trimoxazole 960mg once a day on Mondays, Wednesdays and Fridays. Please supply 28 days. This may be dispensed as 480mg twice a day on Mondays, Wednesdays and Fridays according to local practice.

19. Aciclovir 400mg twice a day for 28 days oral
   Administration Information
   Please supply 28 days or an original pack if appropriate

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

21. Gastric Protection
   Administration Information
   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 dispense 28 days or nearest original pack size.

Cycles 2 - 12, Days 1, 2, 8, 9, 15, 16

22. Dexamethasone 20mg oral 30 minutes prior to the carfilzomib
   Administration Instructions
   Administer at least 30 minutes and up to four hours prior to the start of the carfilzomib infusion

23. Carfilzomib 56mg/m² (maximum 123mg) intravenous infusion in 100ml glucose 5% over 30 minutes

24. Chlorphenamine 10mg intravenous injection once only when required for infusion related reactions.

25. Hydrocortisone 100mg intravenous injection once only when required for infusion related reactions

26. Salbutamol 2.5mg nebule once only when required for infusion related bronchospasm

27. Paracetamol 1000mg oral once only when required for infusion related reactions
   Administration Instructions
   Please check if the patient has taken paracetamol. Maximum dose is 4g per 24 hours. There should be 4 hours between doses
Take home medicines (Cycles 2-12, Day 1 only)

28. Dexamethasone 20mg once a day on day 22 and 23 oral
   Administration Information
   Please supply two doses of dexamethasone on day 1 of the cycle, ONE dose to be taken on day 22 and on day 23 of the cycle, once a day in the morning
   Take with or after food.

29. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday for 28 days oral
   Administration Instructions
   Co-trimoxazole 960mg once a day on Mondays, Wednesdays and Fridays. Please supply 28 days. This may be dispensed as 480mg twice a day on Mondays, Wednesdays and Fridays according to local practice.

30. Aciclovir 400mg twice a day for 28 days oral
   Administration Instructions
   Please supply 28 days or an original pack if appropriate

31. 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 dispense 28 days or nearest original pack size.
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 protocols should be used in conjunction with other references such as the Summary of Product Characteristics and relevant published papers.