Chemotherapy Protocol

MULTIPLE MYELOMA

VTD-pace (IV)-BOREZOMIB (IV)-CISPLATIN-CYCLOPHOSPHAMIDE-DEXAMETHASONE-DOXORUBICIN-ETOPOSIDE-THALIDOMIDE

(VTD-pace IV)

In-Patient Regimen

There are multiple versions of this protocol in use. Please ensure you have the correct protocol for the relevant diagnosis.

Regimen

- Multiple Myeloma– InP-VTD-pace (IV)-Bortezomib (IV)-Cisplatin-Cyclophosphamide-Dexamethasone-Doxorubicin-Etoposide-Thalidomide (VDT-pace SC)

Indication

- Multiple myeloma in selected patients of good performance status with resistant disease, particularly where urgent disease control is required.

Toxicity

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adverse Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bortezomib</td>
<td>GI disturbances, peripheral neuropathy, hypotension, dizziness, blurred vision, headache, musculoskeletal pain, pyrexia</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>Renal impairment, hearing loss, peripheral neuropathy</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>Dysuria, haemorrhagic cystitis (rare), taste disturbances</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>Weight gain, gastro-intestinal disturbances, hyperglycaemia, CNS disturbances, cushingoid changes, glucose intolerance</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>Cardiomyopathy, alopecia, urinary discoulouration (red),</td>
</tr>
<tr>
<td>Etoposide</td>
<td>Hypotension on rapid infusion, alopecia, hyperbilirubinaemia</td>
</tr>
<tr>
<td>Thalidomide</td>
<td>Drowsiness, constipation, dizziness, increased risk of thromboembolic events, dry skin/rash, peripheral neuropathy, teratogenicity, syncope, bradycardia</td>
</tr>
</tbody>
</table>

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 (including calcium and magnesium) prior to day one of treatment. FBC should be assessed frequently as blood products are often required.

- Regular blood glucose monitoring is considered good practice

- Ensure adequate cardiac function before starting therapy. Baseline LVEF should be measured in patients with a history of cardiac problems, cardiac risk factors or in the elderly. Discontinue doxorubicin if cardiac failure develops

- Paraprotein or light chains every 3 weeks

- Pregnancy testing in women of childbearing potential. A negative pregnancy test must be obtained within 3 days of starting thalidomide the test must be repeated every 4 weeks (every 2 weeks in women with irregular menstrual cycles) with the final test 4 weeks after the last dose of thalidomide.

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and limited drug specific toxicities. 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 erythropoietins if the patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL.

Haematological modifications are not necessary for dexamethasone or thalidomide.

<table>
<thead>
<tr>
<th>Neutrophils (x10⁹/L)</th>
<th>Platelets (x10⁹/L)</th>
<th>Dose Modifications (bortezomib, cisplatin, cyclophosphamide, doxorubicin and etoposide)</th>
</tr>
</thead>
<tbody>
<tr>
<td>greater than or equal to 1 and</td>
<td>greater than or equal to 75</td>
<td>100%</td>
</tr>
<tr>
<td>less than 1 and / or</td>
<td>less than 75</td>
<td>Consider delay until recovery</td>
</tr>
</tbody>
</table>
In the presence of cytopenias due to marrow involvement with myeloma it is possible that the cycle 1 day 1 dose will proceed even if the neutrophils are less than 1 and the platelets less than 75. This should be confirmed with the consultant.

**Hepatic Impairment**

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Bilirubin (μmol/L)</th>
<th>AST/ALT (units/L)</th>
<th>Dose (% of original dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bortezomib</td>
<td>1.5xULN or below</td>
<td>N/A</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>greater than 1.5xULN</td>
<td>N/A</td>
<td>Initiate treatment at 0.7mg/m². The dose may be escalated to 1mg/m² or reduced to 0.5mg/m² in subsequent cycles based on patient tolerability.</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>N/A</td>
<td>N/A</td>
<td>No dose modification required</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>more than 30</td>
<td>2-3xULN</td>
<td>Clinical decision. Evidence that exposure to active metabolites may not be increased, suggesting dose reduction may not be necessary</td>
</tr>
<tr>
<td></td>
<td>and/or</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>30-50</td>
<td>More than 3xULN</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>51-85</td>
<td>N/A</td>
<td>25%</td>
</tr>
<tr>
<td></td>
<td>more than 85</td>
<td>N/A</td>
<td>omit</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>less than 30</td>
<td>2-3xULN</td>
<td>75%</td>
</tr>
<tr>
<td></td>
<td>and/or</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>30-50</td>
<td>More than 3xULN</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>51-85</td>
<td>N/A</td>
<td>25%</td>
</tr>
<tr>
<td></td>
<td>more than 85</td>
<td>N/A</td>
<td>omit</td>
</tr>
<tr>
<td>Etoposide</td>
<td>30-51</td>
<td>60-180</td>
<td>Consider dose reducing to 50%</td>
</tr>
<tr>
<td></td>
<td>and/or</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>30-51</td>
<td>More than 180</td>
<td>Clinical decision</td>
</tr>
<tr>
<td></td>
<td>more than 51</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thalidomide</td>
<td>N/A</td>
<td>N/A</td>
<td>No dose modification required</td>
</tr>
</tbody>
</table>

*ULN indicates upper limit of normal.*
### Renal Impairment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Creatinine Clearance (ml/min)</th>
<th>Dose (% of original dose)</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bortezomib</td>
<td>greater than 20</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>20 and below</td>
<td>Clinical decision</td>
<td></td>
</tr>
<tr>
<td>Cisplatin*</td>
<td>more than 50</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>40-50</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>less than 40</td>
<td>omit</td>
<td></td>
</tr>
<tr>
<td>Cyclophosphamide**</td>
<td>more than 20</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10-20</td>
<td>75%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>less than 10</td>
<td>omit</td>
<td></td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>less than 10</td>
<td>Consider dose reduction in severe renal failure</td>
<td></td>
</tr>
<tr>
<td>Etoposide</td>
<td>more than 50</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>15-50</td>
<td>75%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Less than 15</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>Thalidomide</td>
<td>N/A</td>
<td>No dose modification required</td>
<td></td>
</tr>
</tbody>
</table>

*Consider carboplatin as an alternative to cisplatin at a dose of 50mg/m² per day for four days if the creatinine clearance is less than 40ml/min.

**Consider mesna in patients with pre-existing bladder disorders. Give an oral dose of 40% of the cyclophosphamide dose (rounded upwards to the nearest 400mg) at 0, 2 and 6 hours after the administration of the cyclophosphamide.

**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 1mg/m$^2$ or switch to a weekly bortezomib at the standard dose of 1.3mg/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 0.7mg/m$^2$. For NCI-CTC grade 4 neuropathy and/or severe autonomic neuropathy discontinue bortezomib.

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

Doxorubicin

Discontinue doxorubicin if cardiac failure develops

Etoposide

Where significant reductions in albumin levels occur consider reducing the dose of etoposide.

Thalidomide

Peripheral Neuropathy

If NCI-CTC grade 1 neurological toxicity occurs treatment may be continued, if symptoms worsen consider dose reduction or interruption. Treatment may be reintroduced at a reduced dose if symptoms resolve. If NCI-CTC grade 2 neurological toxicity occurs suspend treatment or reduce the dose by at least 50%. Treatment may be reintroduced at a reduced dose if symptoms resolve to grade 1 or below. For NCI-CTC neurological toxicity grade 3 or above or toxicity that does not resolve despite treatment interruption / dose reduction thalidomide treatment should be stopped.

Thromboembolism

The thrombotic risk for patients commencing on thalidomide must be assessed. Appropriate thromboprophylaxis must be prescribed according to local policies. Thromboprophylaxis is generally recommended for at least the first 5 months of thalidomide treatment, especially in patients with additional thrombotic risk factors. Patients and their carers should be made aware of the risk and thrombosis should be sought promptly.
aware of the symptoms of thromboembolism and advised to report sudden breathlessness, chest pain, or swelling of a limb.

The occurrence of a thromboembolic event such as a DVT or thromboembolism, notably pulmonary embolism, is an indication for full anticoagulation following standard treatment guidelines. Thalidomide may be stopped, but can be re-introduced, initially at 50mg daily with escalation at subsequent cycles to 100mg, assuming good anticoagulant control and no other untoward side effects.

All patients should be initially prescribed a low molecular weight heparin at the appropriate prophylactic dose. Therapeutic warfarin is an alternative to low molecular heparin. Aspirin 75mg each morning is an alternative in very low risk patients once a response has been obtained.

*Teratogenicity*

Thalidomide is highly teratogenic.

All prescribers, patients and pharmacy staff must comply with the manufacturer’s Pregnancy Prevention Programme.

Women of child-bearing potential taking thalidomide must use one agreed effective method of contraception for at least 4 weeks before starting thalidomide, while on thalidomide and for one month after. They must have a negative pregnancy test within 3 days prior to starting treatment. Pregnancy testing should be repeated monthly thereafter until one month after stopping thalidomide (or every 2 weeks in women with irregular menstrual cycles). If a woman taking thalidomide thinks she may be pregnant she must stop the drug immediately and seek medical advice.

Men taking thalidomide must use a barrier method of contraception throughout treatment and for one week after stopping, if their partner is capable of bearing children.

*Other*

For other thalidomide related toxicities of NCI-CTC grade 3 or above. Stop thalidomide until recovery to NCI-CTC grade 1 or below. Cautious reintroduction of thalidomide at a dose of 50mg a day may be considered with dose escalation if tolerated.

*Regimen*

The dose of bortezomib in this protocol is higher than that of other versions used. Check with the appropriate consultant that this is appropriate.

The dose of thalidomide is set to increase on cycle two. This is optional. Please refer to the appropriate consultant for advice.
## 21 day cycle for up to 3 cycles

### Cycle 1

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Days</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bortezomib</td>
<td>1.3mg/m²</td>
<td>1, 4, 8, 11</td>
<td>Intravenous injection over 5 seconds</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>10mg/m²/day</td>
<td>1, 2, 3, 4</td>
<td>Continuous intravenous infusion in 1000ml sodium chloride 0.9% over 24 hours or via a portable infusion device</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>400mg/m²/day</td>
<td>1, 2, 3, 4</td>
<td>Intravenous infusion in 1000ml sodium chloride 0.9% over 24 hours or via a portable infusion device</td>
</tr>
<tr>
<td>Etoposide</td>
<td>40mg/m²/day</td>
<td>1, 2, 3, 4</td>
<td></td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>10mg/m²/day</td>
<td>1, 2, 3, 4</td>
<td>Intravenous infusion in 1000ml sodium chloride 0.9% over 24 hours or via a portable infusion device</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>40mg</td>
<td>1, 2, 3, 4</td>
<td>Oral</td>
</tr>
<tr>
<td>Thalidomide</td>
<td>50mg once a day at night</td>
<td>1-21 incl.</td>
<td>Oral</td>
</tr>
</tbody>
</table>

### Cycle 2, 3

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Days</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bortezomib</td>
<td>1.3mg/m²</td>
<td>1, 4, 8, 11</td>
<td>Intravenous injection over 5 seconds</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>10mg/m²/day</td>
<td>1, 2, 3, 4</td>
<td>Continuous intravenous infusion in 1000ml sodium chloride 0.9% over 24 hours or via a portable infusion device</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>400mg/m²/day</td>
<td>1, 2, 3, 4</td>
<td>Intravenous infusion in 1000ml sodium chloride 0.9% over 24 hours or via a portable infusion device</td>
</tr>
<tr>
<td>Etoposide</td>
<td>40mg/m²/day</td>
<td>1, 2, 3, 4</td>
<td></td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>10mg/m²/day</td>
<td>1, 2, 3, 4</td>
<td>Intravenous infusion in 1000ml sodium chloride 0.9% over 24 hours or via a portable infusion device</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>40mg</td>
<td>1, 2, 3, 4</td>
<td>Oral</td>
</tr>
<tr>
<td>Thalidomide</td>
<td>100mg once a day at night</td>
<td>1-21 incl.</td>
<td>Oral</td>
</tr>
</tbody>
</table>

### Dose Information

- Bortezomib will be dose banded according to the agreed bands
- Cisplatin will be dose banded according to the agreed bands
- Cyclophosphamide will be dose banded according to the agreed bands
- Doxorubicin will be dose banded according to the agreed bands
• The maximum lifetime cumulative dose of doxorubicin is 450mg/m². However prior radiotherapy to mediastinal/pericardial area should receive a lifetime cumulative doxorubicin dose of no more than 400mg/m²

• Etoposide will be dose banded according to the agreed bands

• Dexamethasone is available as 2mg and 500mcg tablets

• Thalidomide is available as 50mg capsules

Administration Information

Extravasation

• Bortezomib - neutral

• Cisplatin – exfoliant

• Cyclophosphamide – neutral

• Doxorubicin – vesicant

• Etoposide - irritant

Other

• Dexamethasone should be taken in the morning with or after food. Administration of prednisolone begins on the morning of chemotherapy.

• Thalidomide should be taken at night to avoid daytime drowsiness

• A central catheter or PICC line is advised for administration of this regimen

Additional Therapy

• Antiemetics

  Starting 15-30 minutes prior to chemotherapy
  - metoclopramide 10mg oral or intravenous
  - ondansetron 8mg oral or intravenous

Thereafter
  - metoclopramide 10mg three times a day for 5 days oral or intravenous
  - ondansetron 8mg twice a day for 5 days oral or intravenous

• Thromboprophylaxis according to local formulary choice (if platelets greater than 50x10^9/L). For example;

  - dalteparin 5000units once a day subcutaneous injection
  - enoxaparin 40mg once a day subcutaneous injection
  - heparin 5000units twice a day subcutaneous injection
• Anti-infective prophylaxis with
  - aciclovir 400mg twice a day oral
  - ciprofloxacin 250mg twice a day oral
  - co-trimoxazole 960mg once a day on Monday, Wednesday or Friday oral or
  - consider pentamidine nebuliser 300mg every four weeks
  - fluconazole 100mg once a day oral

• Consider allopurinol 300mg once a day for seven days for cycle one only

• Consider growth factors according to local formulary choice starting on day five of the cycle and continuing until the neutrophils are greater than 1x10^9/L.

• Mouthcare for the prophylaxis or treatment of mucositis in accordance with local guidelines

• Laxatives as required for thalidomide-induced constipation.

• Bisphosphonates in accordance with local policies

• 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.

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.

• For all patients taking thalidomide; the patient, prescriber, and supplying pharmacy must comply with an appropriate pregnancy prevention programme.

• Every thalidomide prescription must be accompanied by a complete Prescription Authorisation Form.

Coding

• Procurement – X71.5, X72.4

• Delivery – not applicable

References
REGIMEN SUMMARY

InP- VTD-PACE (IV)-Bortezomib (IV)-Cisplatin-Cyclophosphamide-Dexamethasone-Doxorubicin-Etoposide-Thalidomide

Other than those listed below, orally administered ACTIVE and all supportive medication for this regimen will not appear in Aria as prescribed agents. The administration instructions for each warning describes the agents which must be prescribed on the in-patient chart or general electronic prescribing system

Cycle 1 Day 1

1. Warning – Check ACTIVE/supportive meds prescribed
   Administration Instructions
   Active and supportive treatments to be written on the in-patient chart, all starting on day 1:
   1. Dexamethasone 40mg once a day in the morning days 1, 2, 3, 4 orally
   2. Thalidomide 50mg once a day at night for 21 nights – Pregnancy Prevention Programme. Oral chemotherapy
   3. Metoclopramide 10mg oral or intravenous followed by 10mg three times a day for five days oral or intravenous
   4. Ondansetron 8mg oral or intravenous followed by 8mg twice a day for five days oral or intravenous
   5. Aciclovir 400mg twice a day for 21 days oral
   6. Ciprofloxacin 250mg twice a day for 21 days oral
   7. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday only or pentamidine nebulus
   8. Fluconazole 100mg once a day for 21 days oral
   9. Thromboprophylaxis according to local formulary choice for 21 days. For example;
      - dalteparin 5000units once a day subcutaneous injection
      - enoxaparin 40mg once a day subcutaneous injection
      - heparin 5000units twice a day subcutaneous injection
   10. Consider allopurinol 300mg once a day for 7 days for cycle 1 only.
   11. Consider growth factors starting on day 5 according to local formulary choice
   12. Mouthcare according to local guidelines
   13. Hydration as per local guidelines

2. Doxorubicin 10mg/m²/day intravenous infusion in 1000ml sodium chloride 0.9% over 24 hours

3. Cisplatin 10mg/m²/day, cyclophosphamide 400mg/m²/day, etoposide 40mg/m²/day intravenous infusion in 1000ml sodium chloride 0.9% over 24 hours

4. Bortezomib 1.3mg/m² intravenous injection over 5 seconds
   Administration Instruction
   The dose of bortezomib in this protocol differs from that used in other hospitals. Check with the appropriate consultant before prescribing.

Cycle 1 Day 2, 3

5. Doxorubicin 10mg/m²/day intravenous infusion in 1000ml sodium chloride 0.9% over 24 hours

6. Cisplatin 10mg/m²/day, cyclophosphamide 400mg/m²/day, etoposide 40mg/m²/day intravenous infusion in 1000ml sodium chloride 0.9% over 24 hours

Cycle 1 Day 4

7. Doxorubicin 10mg/m²/day intravenous infusion in 1000ml sodium chloride 0.9% over 24 hours
8. Cisplatin 10mg/m²/day, cyclophosphamide 400mg/m²/day, etoposide 40mg/m²/day intravenous infusion in 1000ml sodium chloride 0.9% over 24 hours

9. Bortezomib 1.3mg/m² intravenous injection over 5 seconds
   Administration Instruction
   The dose of bortezomib in this protocol differs from that used in other hospitals. Check with the appropriate consultant before prescribing.

**Cycle 1 day 8, 11 (may be given as out-patient)**

10. Bortezomib 1.3mg/m² intravenous injection over 5 seconds
    Administration Instruction
    The dose of bortezomib in this protocol differs from that used in other hospitals. Check with the appropriate consultant before prescribing.

**Cycles 2 and 3 Day 1**

11. Warning – Check ACTIVE/ supportive meds prescribed
    Administration Instructions
    Active and supportive treatments to be written on the in-patient chart, all starting on day 1:
    1. Dexamethasone 40mg once a day in the morning days 1, 2, 3, 4 orally
    2. Thalidomide 100mg once a day at night for 21 nights – Pregnancy Prevention Programme. Oral chemotherapy
    3. Metoclopramide 10mg oral or intravenous followed by 10mg three times a day for five days oral or intravenous
    4. Ondansetron 8mg oral or intravenous followed by 8mg twice a day for five days oral or intravenous
    5. Aciclovir 400mg twice a day for 21 days oral
    6. Ciprofloxacin 250mg twice a day for 21 days oral
    7. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday only or pentamidine nebules
    8. Fluconazole 100mg once a day for 21 days oral
    9. Thromboprophylaxis according to local formulary choice for 21 days. For example;
       - dalteparin 5000units once a day subcutaneous injection
       - enoxaparin 40mg once a day subcutaneous injection
       - heparin 5000units twice a day subcutaneous injection
    10. Consider growth factors starting on day 5 according to local formulary choice
    11. Mouthcare according to local guidelines
    12. Hydration as per local guidelines

12. Doxorubicin 10mg/m²/day intravenous infusion in 1000ml sodium chloride 0.9% over 24 hours

13. Cisplatin 10mg/m²/day, cyclophosphamide 400mg/m²/day, etoposide 40mg/m²/day intravenous infusion in 1000ml sodium chloride 0.9% over 24 hours

14. Bortezomib 1.3mg/m² intravenous injection over 5 seconds
    Administration Instruction
    The dose of bortezomib in this protocol differs from that used in other hospitals. Check with the appropriate consultant before prescribing.

**Cycles 2 and 3 Day 2, 3**

15. Doxorubicin 10mg/m²/day intravenous infusion in 1000ml sodium chloride 0.9% over 24 hours

16. Cisplatin 10mg/m²/day, cyclophosphamide 400mg/m²/day, etoposide 40mg/m²/day intravenous infusion in 1000ml sodium chloride 0.9% over 24 hours
Cycles 2 and 3 Day 4

17. Doxorubicin 10mg/m²/day intravenous infusion in 1000ml sodium chloride 0.9% over 24 hours

18. Cisplatin 10mg/m²/day, cyclophosphamide 400mg/m²/day, etoposide 40mg/m²/day intravenous infusion in 1000ml sodium chloride 0.9% over 24 hours

19. Bortezomib 1.3mg/m² intravenous injection over 5 seconds
   Administration Instruction
   The dose of bortezomib in this protocol differs from that used in other hospitals. Check with the appropriate consultant before prescribing.

Cycles 2 and 3 Day 8, 11 (may be given as out-patient)

20. Bortezomib 1.3mg/m² intravenous injection over 5 seconds
   Administration Instruction
   The dose of bortezomib in this protocol differs from that used in other hospitals. Check with the appropriate consultant before prescribing.
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 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.