DT-PACE (dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide and etoposide) for Myeloma

Indication: Relapsed / refractory Multiple Myeloma

Regimen details:
- **Dexamethasone**: 40 mg PO Days 1 to 4
- **Thalidomide**: 100 to 200 mg PO Days 1 to 28
- **Cisplatin**: 10 mg/m² IV Days 1 to 4
- **Doxorubicin**: 10 mg/m² IV Days 1 to 4
- **Cyclophosphamide**: 400 mg/m² IV Days 1 to 4
- **Etoposide**: 40 mg/m² IV Days 1 to 4

Administration:
- Dexamethasone orally
- Thalidomide orally
- Cisplatin, cyclophosphamide and etoposide IV infusion in 1000ml sodium chloride 0.9% over 24 hours
- Doxorubicin IV infusion in 100ml sodium chloride 0.9% over 24 hours

Premedication: None required

Frequency: Up to 3 cycles. Repeat after 28 days as soon as blood count recovery.

Extravasation: Doxorubicin is a vesicant and cisplatin is an irritant. Administer with appropriate precautions to prevent extravasation.
If there is any possibility that extravasation has occurred, contact a senior member of the medical team and follow local protocol for dealing with cytotoxic extravasation of irritant and non-vesicant drugs.

Anti-emetics: High emetogenic potential (>90%). Antiemetics as per local policy.

Supportive medication:
- Allopurinol 300mg od orally (100mg if renal impairment) for prevention of tumour lysis syndrome for first cycle only.
- PPI prophylaxis e.g. omeprazole 20mg od orally.
- Mouthcare e.g. sodium Chloride 0.9% mouthwash, 10ml qds
- Antimicrobial prophylaxis as per local guidelines.
- GCSF support as per local guidelines
- Hydration to run concurrently with the 24 hour chemotherapy infusions: 1000ml sodium chloride 0.9% + 20mmol potassium chloride + 1g magnesium sulphate over 24 hours
- Thromboprophylaxis: All patients should receive thromboprophylaxis with aspirin 75mg od unless contraindicated. Patients with a previous VTE or who are at high risk of VTE (one other risk factor in addition to multiple myeloma) should receive LMWH e.g. enoxaparin 40mg sc od as per local protocol.
- Prophylactic laxatives as per local protocol

Regular investigations:
- **Baseline & regular**
  - FBC Prior to day 1
  - LFTs Prior to day 1
  - U&Es Prior to day 1
  - Serum paraprotein and serum free light chains at the start of each cycle
Blood pregnancy test for women of child bearing potential within 3 days of the prescription date for every cycle.
Virology screen – Hep B & C, HIV prior to initiating treatment (Hep B includes HBsAg and HBcAb)

**Dose Modifications**

**Haematological Toxicity**

Prior to day 1:

<table>
<thead>
<tr>
<th>Neutrophils (x 10⁹/L)</th>
<th>Platelets (x 10⁹/L)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1.0 x 10⁹/L &amp; ≥100 x 10⁹/L</td>
<td>100% dose</td>
<td></td>
</tr>
<tr>
<td>&lt; 1.0 x 10⁹/L &amp; / or &lt; 100 x 10⁹/L</td>
<td>Hold until recovery</td>
<td></td>
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</tbody>
</table>

NB. In the presence of cytopenias due to marrow involvement with myeloma, it is possible that the cycle 1 day 1 dose will go ahead even if neutrophils <1.0 x 10⁹/L and platelets < 100 x 10⁹/L. This should be confirmed with a Consultant.

**Renal Impairment**

<table>
<thead>
<tr>
<th>CrCl (ml/min)</th>
<th>Cisplatin Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 50</td>
<td>Give 100%</td>
</tr>
<tr>
<td>30 – 50</td>
<td>Give 50% of the dose</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CrCl (ml/min)</th>
<th>Etoposide Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 50</td>
<td>Give 100%</td>
</tr>
<tr>
<td>30 – 50</td>
<td>Give 75% of the dose</td>
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</tbody>
</table>

For CrCl > 30 ml/min, 100% cyclophosphamide and doxorubicin.

For CrCl < 30m/min, discuss with Consultant regarding administering this regimen.

**Hepatic Impairment**

<table>
<thead>
<tr>
<th>Bilirubin (umol/L)</th>
<th>Modification</th>
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</thead>
<tbody>
<tr>
<td>26 - 51</td>
<td>50% doxorubicin</td>
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</tbody>
</table>

Toxicities: General toxicities: Nausea, vomiting, myelosuppression, mucositis, alopecia, impaired glucose tolerance (high dose steroids), renal dysfunction, ototoxicity.
Thalidomide: thrombosis, somnolence, skin dryness, constipation, sensory peripheral neuropathy, uncommonly motor neuropathy.
Doxorubicin: Consider ECG and echocardiogram/MUGA scan to assess LV function particularly in patients with symptoms and/or signs suggestive of cardiac dysfunction.
If the LV ejection fraction is < 30% - 40%, discuss with Consultant Haematologist and consider omitting doxorubicin.
The maximum cumulative lifetime dose is 450mg/m²
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Drug interactions: If possible, avoid any other potentially nephrotoxic drugs.

Comments: Thalidomide must only be prescribed according to the Pregnancy Prevention Programme. Patients are required to complete an informed consent process.