ESHAP (etoposide, methylprednisolone, cytarabine & cisplatin) for Myeloma

Page 1 of 2

Indication: Relapsed / refractory Multiple Myeloma (for stem cell harvest)

Regimen details:
- Etoposide 40 mg/m² IV Days 1 to 4
- Methylprednisolone 500 mg IV Days 1 to 5
- Cytarabine 2000 mg/m² IV Day 1
- Cisplatin 25 mg/m² IV Days 1 to 4

Administration:
- Etoposide IV infusion in 250-500ml sodium chloride 0.9% over 60 minutes
- Methylprednisolone IV infusion in 100ml sodium chloride 0.9% over 30 minutes
- Cytarabine IV infusion in 500ml sodium chloride 0.9% over 2 hours
- Cisplatin IV infusion in 1000ml sodium chloride 0.9% over 24 hours. Pre- and post- hydration is required, please see information in supportive medication section below.

Premedication: None required

Frequency: Up to 2 cycles. Repeat after 21 to 28 days as soon as blood count recovery. (Stem cell mobilisation may occur after the first or second cycle).

Extravasation: Cisplatin is an irritant and should be administered 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%) e.g. ondansetron 16mg orally prior to chemotherapy and ondansetron 16mg orally the day after and metoclopramide 20mg orally tds for 3 days after chemotherapy.

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
Pre- cisplatin hydration: 1000ml sodium chloride 0.9% over 2 hours
Commence cisplatin when urine output > 100ml/hour
Post- cisplatin hydration: 1000ml sodium chloride 0.9% + 20mmol potassium chloride + 1g magnesium sulphate over 18 hours and 30 minutes (i.e. runs concurrently with cisplatin)
Furosemide 40mg orally
Steroid eye drops e.g. Predsol 0.5%, 1 drop both eyes every 2 hours for 4 days
Antimicrobial prophylaxis as per local guidelines.
GCSF support as per local guidelines.
ESHAP (etoposide, methylprednisolone, cytarabine & cisplatin) for Myeloma

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

Virology screen – Hep B & C, HIV prior to initiating treatment (Hep B includes HBsAg and HBcAb)

**Reason for Update:** 2 year review

Approved by Consultant: M Streetly 27/03/2013
Approved by Chair Haem TWG: M Kazmi
Date: 19/04/2013
Checked by (Principal Pharmacist): J Turner 15/04/2013

**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</td>
<td>≥ 100 x 10⁹/L</td>
<td>100% dose</td>
</tr>
<tr>
<td>&lt; 1.0 x 10⁹/L</td>
<td>&lt; 100 x 10⁹/L</td>
<td>Hold until recovery.</td>
</tr>
</tbody>
</table>

Doses reduced for haematological toxicity should continue for subsequent cycles.

**Renal Impairment**

<table>
<thead>
<tr>
<th>CrCl (ml/min)</th>
<th>Cisplatin Dose</th>
<th>Cytarabine Dose</th>
<th>Etoposide Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 60</td>
<td>Give 100%</td>
<td>Give 100%</td>
<td>Give 100%</td>
</tr>
<tr>
<td>40 – 60</td>
<td>Give 50% of the dose</td>
<td>Give 60% of the dose</td>
<td>Give 75% of the dose</td>
</tr>
<tr>
<td>&lt; 40</td>
<td>Omit and discuss with Consultant</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Hepatic Impairment**

<table>
<thead>
<tr>
<th>Bilirubin (umol/L)</th>
<th>Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 50</td>
<td>50% Cytarabine dose and omit etoposide</td>
</tr>
</tbody>
</table>

**Toxicities:** Nausea, vomiting, severe myelosuppression, mucositis, alopecia, impaired glucose tolerance (high dose steroids), renal dysfunction, ototoxicity.

**Drug interactions:** If possible, avoid any other potentially nephrotoxic drugs.

**Comments:** Renal function should be assessed by EDTA clearance before prescribing. Monitor trends in serum creatinine between treatments: if > 25% from baseline value re-calculate using the Cockcroft & Gault equation.

Weight should be recorded prior to and at the end of cisplatin treatment, and a strict fluid balance chart should be maintained. An average urine output of at least 100ml/hour must be maintained throughout treatment and cisplatin infusion should not be commenced unless this urine output is achieved. For low urine output consider increasing the pre-hydration and diuretic regimen. Consider adding diuretics in weight-gain of 1.5kg or symptoms of fluid overload.

**References:** D’Sa S et al. Etoposide, methylprednisolone, cytarabine and cisplatin successfully cytoreduces resistant myeloma patients and mobilizes them for transplant without adverse effects. Br J Haematol 2004; 125: 756-765