**MEC (Mitoxantrone, Etoposide & Cytarabine) for relapsed / refractory AML**

**Indication:** Relapsed / refractory acute myeloid leukaemia

**Regimen details:**
- **Mitoxantrone**: 8mg/m² IV Days 1 to 5
- **Etoposide**: 100mg/m² IV Days 1 to 5
- **Cytarabine**: 1000mg/m² IV Days 1 to 5

**Administration:**
- Mitoxantrone: IV infusion in 50-100ml sodium chloride 0.9% over 20 minutes
- Etoposide: IV infusion in sodium chloride 0.9% over 1 hour. Etoposide infusion should have a maximum concentration of 0.2 - 0.35mg/mL (PVC free).
- Monitor etoposide infusion for the first 15 minutes for signs of hypotension.
- Cytarabine: IV infusion over 4 hours

**Premedication:** None required

**Frequency:** 1 or 2 cycles
Proceed with the next cycle when neutrophils \( \geq 1.0 \times 10^9/L \) and platelets \( \geq 100 \times 10^9/L \)

**Extravasation:** Mitoxantrone and Etoposide are irritants.
Cytarabine is not a vesicant.

**Anti-emetics:**
- Cytarabine: high emetogenicity
- Mitoxantrone: moderate emetogenicity
- Etoposide: low emetogenicity
Follow local anti-emetic policy

**Supportive medication:** Rasburicase or allopurinol for prevention of tumour lysis syndrome as per local policy for cycle 1 only.

**Mouthcare**
- Antimicrobial prophylaxis whilst neutrophil count < 0.5 x 10⁹/L as per local policy.
- Corticosteroid eye drops as per local formulary (e.g. prednisolone (Predsol®) 0.5% or dexamethasone (Maxidex®) 0.1%), during and for 3 days after completion of chemotherapy

**Regular investigations:** Prior to day 1:
- FBC
- LFTs
- U&Es

**Bone marrow aspirate and trephine at day 18 – 21.**
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Dose Modifications

Haematological Toxicity

Blood counts do not have to be normal prior to cycle 1 MEC

Cycle 2 can go ahead after the response to the first course has been assessed i.e. bone marrow aspirate, neutrophil and platelet count recovery. See under frequency.

Renal Impairment

No dose reductions are required for mitoxantrone

<table>
<thead>
<tr>
<th>Creatinine Clearance (mL/min)</th>
<th>Etoposide</th>
<th>Cytarabine</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 50</td>
<td>100% dose</td>
<td>100% dose</td>
</tr>
<tr>
<td>15 - 50</td>
<td>75% dose</td>
<td>60% dose</td>
</tr>
<tr>
<td>&lt; 15</td>
<td>50% dose</td>
<td>50% dose</td>
</tr>
</tbody>
</table>

Hepatic Impairment

No dose reductions are required for mitoxantrone

<table>
<thead>
<tr>
<th>Bilirubin (µmol/L)</th>
<th>AST (units / L)</th>
<th>Etoposide</th>
</tr>
</thead>
<tbody>
<tr>
<td>26 - 51 or 60 - 180</td>
<td>50% dose</td>
<td></td>
</tr>
<tr>
<td>&gt; 51 or &gt; 180</td>
<td>Consultant decision / Omit</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bilirubin (µmol/L)</th>
<th>Cytarabine</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 34</td>
<td>100% dose</td>
</tr>
<tr>
<td>&gt; 34</td>
<td>50% dose</td>
</tr>
</tbody>
</table>

The dose information for renal and hepatic impairment above is a guide only. Discuss any dose reductions for either renal or hepatic impairment with Consultant because in some circumstances 100% dose may be given.

Toxicities:

Mitoxantrone: may cause urine, saliva, tears and sweat to turn blue-green for 24 hours post infusion. Whites of eyes may have a blue-green tinge (this is normal). Arrhythmias.

Etoposide: Hypotension if infused too fast, alopecia.
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Cytarabine: ocular pain, foreign body sensation, photophobia and blurred vision. Dizziness, headache, confusion, cerebellar toxicity. Skin freckling, itching, cellulites at injection site, rash, skin sloughing of the palmar and plantar surfaces. Myalgia and bone pain

Drug interactions: None applicable

Comments: Maximum cumulative lifetime dose mitoxantrone = 160mg/m²
A baseline MUGA scan or echocardiogram should be performed where the patient is considered at risk of having impaired cardiac function e.g. significant cardiac history, hypertension, obese, smoker, elderly, previous exposure to anthracyclines, previous thoracic radiotherapy.
MUGA scan should be repeated if there is suspicion of cardiac toxicity at any point during treatment, or if cumulative anthracycline dose approaches maximum.

Maximum cumulative lifetime doses of anthracyclines are:
doxorubicin 450 – 550 mg/m²
daunorubicin 500 - 600mg/m²
epirubicin 950mg/m²
idarubicin 93mg/m²
mitoxantrone 160mg/m²

To calculate total exposure to anthracyclines, calculate for each drug the total dose received as a % of the lifetime dose for that drug. Add the % for each drug administered in the past. Maximum lifetime cumulative anthracycline dose is 100%.

References:
Waddell J.A. et al. Mitoxantrone, Etoposide and Cytarabine (MEC) Regimen for Relapsed or Refractory Acute Myelogenous Leukemia. Hospital Pharmacy 2003; 38: 218-221