REGIMEN TITLE: Carboplatin Etoposide IV therapy

Indication: Merkel Cell Carcinoma
Adjuvant and palliative treatment of high risk, unresectable or stage IV disease

Regimen details: Carboplatin AUC 5 (see comments) IV D1
Etoposide 100 mg/m² IV D1 to D3

(Reduced doses or single agent Carboplatin to be considered in elderly patients, Or in patients with poor PS)

Administration: Carboplatin in 500ml Glucose 5% IV over 60 minutes
Etoposide in Sodium Chloride 0.9% IV over 60 min (See comments for volume)

Monitor Etoposide infusion for the first 15 minutes for signs of hypotension.

Frequency: 3 weekly cycle - Day 1 to Day 3.
Total of 4 cycles

Anti- emetics: Day 1. Moderate emetogenicity
Days 2 and 3. Low emetogenicity

Regular investigations: FBC D1
LFTs D1
U&Es D1
EDTA Prior to 1st cycle (see Comments)
Baseline CT
Clinical toxicity assessments (including neuropathy)

Comments: Etoposide infusion should have maximum concentration of 0.2 - 0.4 mg/ml. (PVC free)

Carboplatin dose should be calculated using the Calvert formula:
Dose = Target AUC x (25 + GFR)
GFR should be calculated using the Cockcroft & Gault equation in all patients; if the calculated GFR < 60 or >120ml/min measure EDTA clearance or creatinine clearance before prescribing. EDTA calculation will lead to higher doses than cockroft & Gault equation, so dose adjustment may be required. Monitor trends in serum creatinine between treatments: if >25% from baseline value re-calculate GFR using the Cockcroft & Gault equation.
Extravasation: Non vesicant

Toxicities:
- Nausea and vomiting
- Myelosuppression - risk of sepsis and thrombocytopenia
- Constipation and/or diarrhoea
- Hypotension
- Moderate alopecia
- Peripheral neuropathy
- Neurotoxicity (ototoxicity)
- Nephrotoxicity
- Stomatitis
- Dysgeusia
- Fatigue, ovarian failure/infertility

Anaphylactic reactions have been reported following Etoposide administration.

Adequate contraceptive methods should be used during therapy.

**Dose Modifications**

**Haematological Toxicity**

<table>
<thead>
<tr>
<th>Neutrophils x 10⁹/l</th>
<th>Platelets x 10⁹/l</th>
<th>Carboplatin Dose</th>
<th>Etoposide dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1.5 and ≥100</td>
<td></td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>&lt;1.0 or &lt; 100</td>
<td></td>
<td>Delay*</td>
<td>Delay*</td>
</tr>
</tbody>
</table>

*Delay therapy for 1 week.
Reduce doses for subsequent cycles if febrile neutropenia occurs.

**Renal Impairment**

<table>
<thead>
<tr>
<th>CrCl (mL/min)</th>
<th>Etoposide dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>46-60</td>
<td>85% dose</td>
</tr>
<tr>
<td>30-45</td>
<td>80% dose</td>
</tr>
<tr>
<td>&lt;30</td>
<td>75% dose</td>
</tr>
</tbody>
</table>

Subsequent doses based on clinical response

**Hepatic Impairment**

Carboplatin: No dose modifications for hepatic impairment

<table>
<thead>
<tr>
<th>Bilirubin (micromol/L)</th>
<th>AST (units/L)</th>
<th>Etoposide dose (mg)</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>Clinical decision.</td>
<td></td>
</tr>
</tbody>
</table>

**Drug interactions:**
- Aluminium-containing equipment should not be used during preparation and administration of Carboplatin
- Aminoglycoside antibiotics - increased risk of ototoxicity (with Carboplatin)
- Aprepitant - elevated Etoposide plasma levels
- Cyclosporin (high doses) increase Etoposide plasma levels/toxicity.
- Glucosamine - possible reduced Etoposide effectiveness
- Grapefruit juice - reduced Etoposide plasma levels
- Monitor INR levels carefully if on concomitant warfarin
- Nephrotoxic drugs (with Carboplatin)
- Phenytoin, carbamazepine - Carboplatin decreases efficiency
- St John's Wort - possible reduced Etoposide effectiveness

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**Reason for Update:** Network Protocol development

**Version:** 1

**Supersedes:** All other versions

**Date:** 30/06/09

**Prepared by:** S.Eestila May 08

**Checked by:** (Network Pharmacist): J.Turner

**Approved by SELCN DTAC Chair:** Nic Ketley

**Date:** 15/07/09
References:  
www.medicines.org.uk, accessed April 08
Micromedex review, accessed April 08