Carboplatin / Etoposide for Recurrent Malignant Glioma

Indication: Second line chemotherapy for Recurrent Malignant Glioma

Regimen details: Carboplatin AUC 5 (if C&G) IV D1 (see Comments)
Etoposide 100mg/m² IV D1

OR

Carboplatin AUC 4 (if EDTA) IV D1 (see Comments)
Etoposide 100mg/m² IV D1

Administration: Carboplatin in 500mls Glucose 5% IV over 30-60 minutes
Etoposide in Sodium Chloride 0.9% IV over 60 minutes. Etoposide infusion should have maximum concentration of 0.2 – 0.35 mg/ml (PVC free)
Monitor Etoposide infusion for the first 15 minutes for signs of hypotension

Frequency: Every 28 days, for 4 – 6 cycles

Extravasation: Carboplatin and Etoposide: Non-vesicants

Anti-emetics: Moderate emetogenic. Follow Local Anti-emetic Policy

Regular investigations: FBC D1
LFTs D1
U&Es D1
EDTA Prior to 1st cycle, if necessary (see Comments)
CT scan Prior to 1st cycle and every 2 cycles
Clinical toxicity assessments Each cycle

Comments: 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. Carboplatin dose is calculated as AUC 4, if EDTA is used.
Monitor trends in serum creatinine between treatments: if > 20% from baseline value, recalculate GFR using the Cockcroft & Gault equation

DOSE MODIFICATIONS
Haematological Toxicity

<table>
<thead>
<tr>
<th>Neutrophils</th>
<th>Platelets</th>
<th>Carboplatin / Etoposide Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 1.5 x 10⁹/L and ≥ 150 x 10⁹/L</td>
<td>Give 100%</td>
<td></td>
</tr>
<tr>
<td>1.0 – 1.5 x 10⁹/L and ≥ 150 x 10⁹/L</td>
<td>Give 75%</td>
<td></td>
</tr>
<tr>
<td>&lt; 1.0 x 10⁹/L and &lt; 150 x 10⁹/L</td>
<td>Delay</td>
<td></td>
</tr>
<tr>
<td>&lt; 1.0 x 10⁹/L and ≥ 150 x 10⁹/L</td>
<td>Delay</td>
<td></td>
</tr>
</tbody>
</table>

Reason for Update: Network Protocol Development
Version: 1
Supersedes: All other versions
Prepared by: M.Teresa Pacheca-Palomar Dec ’09
Approved by SELCN DTAC Chair: Date: 24/02/2010
Approved by Brain and CNS Consultant: Lucy Brazil
Date: 03.02.10
Checked by (Network Pharmacist): Jacky Turner
Date: 24/02/2010
Renal Impairment: Carboplatin: Contraindicated if CrCl < 20ml/min

Etoposide dose should be adjusted as follows:

<table>
<thead>
<tr>
<th>CrCl (ml/min)</th>
<th>Etoposide Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 60</td>
<td>Give 100%</td>
</tr>
<tr>
<td>46 – 60</td>
<td>Give 85%</td>
</tr>
<tr>
<td>30 – 45</td>
<td>Give 80%</td>
</tr>
<tr>
<td>&lt; 30</td>
<td>Give 75%</td>
</tr>
<tr>
<td>&lt; 15</td>
<td>Give 50%</td>
</tr>
</tbody>
</table>

Subsequent doses are based on clinical response

Hepatic Impairment: Carboplatin: No dose adjustment required

Etoposide dose should be adjusted as follows:

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

Toxicities: Myelosuppression; peripheral neuropathy (low); nausea; vomiting; mucositis; diarrhoea; nephrotoxicity; ototoxicity (low); alopecia; taste alteration; chills/fever; ovarian failure; infertility

Anaphylactic reactions have been reported following Etoposide administration

Drug interactions: Carboplatin:
- Aluminium-containing equipment should not be used during preparation and administration of Carboplatin
- Aminoglycoside antibiotics: increased risk of nephrotoxicity and ototoxicity
- Clozapine: increased risk of agranulocytosis; avoid concomitant use
- Diuretics: increased risk of nephrotoxicity and ototoxicity
- Nephrotoxic drugs: increased nephrotoxicity; not recommended
- Phenytoin: reduced absorption of the antiepileptic

Etoposide:
- Aprepitant: elevated Etoposide plasma levels
- Ciclosporin (high doses): increased plasma concentration of Etoposide, increased risk of toxicity
- Coumarins: enhanced anticoagulant effect
- Glucosamine; St John’s Wort: possible reduced Etoposide effectiveness
- Grapefruit juice: reduced Etoposide plasma levels
- Phenytoin: reduced absorption of the antiepileptic

References: [www.medicines.org.uk](http://www.medicines.org.uk)
BC Cancer Agency Protocol Summary CNCARV. May 2009
NLCN-Dosage Adjustment for Cytotoxics in Hepatic Impairment. November 2003
NLCN-Dosage Adjustment for Cytotoxics in Renal Impairment. November 2003
GSTT Guidelines for treating Nausea and Vomiting in adult patients. September 2007
CTCAE v3.0. August 2006