Chemotherapy Protocol

GYNAECOLOGICAL CANCER

CARBOPLATIN (AUC5)-ETOPOSIDE

(Intravenous / Oral)

Regimen

- Ovary – Carboplatin (AUC5)-Etoposide IV/PO

Indication

- Small cell or neuroendocrine ovarian cancer
- WHO Performance status 0, 1, 2

Toxicity

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adverse Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin</td>
<td>Neuropathy, hypersensitivity</td>
</tr>
<tr>
<td>Etoposide</td>
<td>Hypotension on rapid infusion, hyperbilirubinaemia</td>
</tr>
</tbody>
</table>

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

Regimen

- EDTA or calculated creatinine clearance before the 1st cycle.
- FBC, LFTs and U&Es prior to each cycle

Dose Modifications

The dose modifications listed are for haematological, liver and renal function only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances. The following is a general guide only.

Haematology

Prior to prescribing on day one of cycle one the following criteria must be met;
Consider blood transfusion if patient symptomatic of anaemia or haemoglobin of less than 8g/dL

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Eligible Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophil</td>
<td>equal to or more than 1x10⁹/L</td>
</tr>
<tr>
<td>Platelets</td>
<td>equal to or more than 100x10⁹/L</td>
</tr>
</tbody>
</table>

### Neutrophils (x10⁹/L)

<table>
<thead>
<tr>
<th>Neutrophils level</th>
<th>Dose Modifications (cisplatin and etoposide)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 or greater</td>
<td>100%</td>
</tr>
<tr>
<td>less than 1</td>
<td>Delay treatment for 7 days. If resolved to 1x10⁹/L or greater after 7 days continue at the full dose</td>
</tr>
</tbody>
</table>

### Platelets (x10⁹/L)

<table>
<thead>
<tr>
<th>Platelets level</th>
<th>Dose Modifications (cisplatin and etoposide)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 or greater</td>
<td>100%</td>
</tr>
<tr>
<td>less than 100</td>
<td>Delay treatment for 7 days. If resolved to 100x10⁹/L or greater after 7 days continue at the full dose</td>
</tr>
</tbody>
</table>

### Hepatic Impairment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Bilirubin µmol/L</th>
<th>AST/ALT units</th>
<th>Dose (% of original dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin</td>
<td>No adjustment necessary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etoposide</td>
<td>26-51 or 60-180</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td></td>
<td>more than 51 or more than 180</td>
<td>clinical decision</td>
<td></td>
</tr>
</tbody>
</table>

### Renal Impairment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Creatinine Clearance (ml/min)</th>
<th>Dose (% of original dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin</td>
<td>Less than 20</td>
<td>Do not use</td>
</tr>
<tr>
<td>Etoposide</td>
<td>more than 50</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>15-50</td>
<td>75</td>
</tr>
<tr>
<td></td>
<td>less than 15</td>
<td>50</td>
</tr>
</tbody>
</table>

### Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.
Regimen

21 day cycle for 6 cycles

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Days</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin</td>
<td>AUC 5</td>
<td>1</td>
<td>Intravenous infusion in 500ml glucose 5% over 60 minutes</td>
</tr>
<tr>
<td>Etoposide</td>
<td>100mg/m²</td>
<td>1</td>
<td>Intravenous infusion in 1000ml sodium chloride 0.9% over 60 minutes</td>
</tr>
<tr>
<td>Etoposide</td>
<td>200mg/m²</td>
<td>2, 3</td>
<td>Oral</td>
</tr>
</tbody>
</table>

Dose Information

- The recommended maximum dose when using a calculated creatinine clearance at AUC5 is 750mg. If you have an obese patient or an individual with a calculated creatinine clearance above 125ml/min please seek advice from the relevant consultant.

- It should be noted that the dose of carboplatin may need to be altered if there is a change (improvement or reduction) in renal function of more than 10% from the previous cycle.

- Carboplatin will be dose rounded to the nearest 50mg (up if halfway)

- Etoposide (intravenous) will be dose banded as per the CSCCN agreed dose bands

- Etoposide (oral) will be dose rounded to the nearest 50mg (up if halfway)

Administration Information

- Etoposide (oral) should be taken an hour before food or on an empty stomach

Extravasation

- Carboplatin – irritant

- Etoposide - irritant

Additional Therapy

- Antiemetics

15-30 minutes prior to chemotherapy;

  - ondansetron 8mg oral or intravenous
  - dexamethasone 8mg oral or intravenous
As take home medication;

- dexamethasone 4mg twice a day oral for 3 days
- metoclopramide 10mg three times a day oral
- ondansetron 8mg twice a day for 3 days

- Gastric protection with a proton pump inhibitor or a H$_2$ antagonist may be considered in patients considered at high risk of GI ulceration or bleed

Additional Information

- The National Patient Safety Agency Alert NPSA/2008/RRR001 must be adhered to in relation to oral etoposide.

Coding

- Procurement – X70.3
- Delivery – X72.1

References

REGIMEN SUMMARY

Carboplatin (AUC5)-Etoposide IV/PO

Day One

1. Dexamethasone 8mg oral or intravenous
2. Ondansetron 8mg oral or intravenous
3. Carboplatin AUC 5 intravenous infusion in 500ml glucose 5% over 60 minutes
4. Etoposide 100mg/m$^2$ intravenous infusion in 1000ml sodium chloride 0.9% over 60 minutes

Take Home Medicines

5. Etoposide 200mg/m$^2$ once a day oral for 2 days starting on day 2 of the chemotherapy cycle
6. Dexamethasone 4mg twice a day oral for 3 days starting on day 2 of the chemotherapy cycle
7. Metoclopramide 10mg three times a day when required oral
8. Ondansetron 8mg twice a day oral for 3 days starting on the evening of day 1 of the chemotherapy cycle
<table>
<thead>
<tr>
<th>Version</th>
<th>Date</th>
<th>Amendment</th>
<th>Written By</th>
<th>Approved By</th>
</tr>
</thead>
</table>
| 1.1     | April 2014 | Carboplatin maximum dose added  
Bolus removed from intravenous bolus  
Metoclopramide dose changed  
OPCS code updated  
Antiemetic start added  
Disclaimer added | Dr Deborah Wright Pharmacist | Donna Kimber Pharmacy Technician |
| 1       | Sept 2013  | None                                                                      | Dr Deborah Wright Pharmacist | Dr C Green Consultant Medical Oncologist  
Dr C Yeoh Consultant Medical Oncologist |

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts:

Hampshire Hospitals NHS Foundation Trust  
NHS Isle of Wight  
Portsmouth Hospitals NHS Trust  
Salisbury Hospital NHS Foundation Trust  
University Hospital Southampton NHS Foundation Trust  
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.