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

Drug	Adverse Effect
Carboplatin	Neuropathy, hypersensitivity
Etoposide	Hypotension on rapid infusion, hyperbilirubinaemia

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;

Criteria	Eligible Level
Neutrophil	equal to or more than $1x10^9$/L
Platelets	equal to or more than $100x10^9$/L

Consider blood transfusion if patient symptomatic of anaemia or haemoglobin of less than 8g/dL

Neutrophils ($x10^9$/L)	Dose Modifications (cisplatin and etoposide)
1 or greater	100%
less than 1	Delay treatment for 7 days. If resolved to $1x10^9$/L or greater after 7 days continue at the full dose
Platelets ($x10^9$/L)	**Dose Modifications (cisplatin and etoposide)**
100 or greater	100%
less than 100	Delay treatment for 7 days. If resolved to $100x10^9$/L or greater after 7 days continue at the full dose

Hepatic Impairment

Drug	Bilirubin µmol/L		AST/ALT units	Dose (%of original dose)
Carboplatin	No adjustment necessary			
Etoposide	26-51	or	60-180	50
	more than 51	or	more than 180	clinical decision

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Carboplatin	Less than 20	Do not use
	Changes in the GFR of more than 10% between cycles may require dose adjustment	
Etoposide	more than 50	100
	15-50	75
	less than 15	50

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

The starting dose of carboplatin AUC 5 is used with calculated GFR. AUC 4 may be considered with EDTA clearance, seek advice from the appropriate consultant before prescribing. The recommended maximum dose when using a calculated creatinine clearance at AUC5 is 750mg (creatinine clearance 125ml/min). This is not a dose included in the national dose banding table. The maximum dose has been set at 790mg in ARIA. Please check if this dose is appropriate. 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.

21 day cycle for 6 cycles

Drug	Dose	Days	Administration
Carboplatin	AUC 5 (max dose)	1	Intravenous infusion in 500ml glucose 5% over 60 minutes
Etoposide	100mg/m^2	1	Intravenous infusion in 1000ml sodium chloride 0.9% over 60 minutes
Etoposide	200mg/m^2	2, 3	Oral

Dose Information

- Carboplatin will be dose banded in accordance with the national dose bands (10mg/ml)
- The maximum dose of carboplatin for AUC 5 is 750mg. This will be set as 790mg in ARIA to comply with national dose bands.
- 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.
- 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.

References
1.Tsolakidis D, Papanikolaou A, Ktenidis K et al. Primary ovarian small cell carcinoma of the pulmonary type with enlarged paraaortic lymph node masses: a case report and review of the literature. Eur J Gynaecol Oncol 2012; 33 (3): 312-315.

REGIMEN SUMMARY

Carboplatin (AUC5)-Etoposide IV/PO

Day One

1. Dexamethasone 8mg oral or intravenous
   Administration Instructions
   Dexamethasone 8mg (or equivalent dose) may be given if the oral route is not appropriate

2. Ondansetron 8mg oral or intravenous
   Administration Instructions
   Ondansetron 8mg may be given if the oral route is not appropriate

3. Warning - Carboplatin Maximum Dose
   Administration Instructions
   The dose of carboplatin is capped at a creatinine clearance of 125ml/min. The internationally recommended maximum dose of carboplatin for AUC 5 is 750mg. The national dose bands do not contain this dose so the cap has been set at 790mg in ARIA. Please check this dose is appropriate for your patient.

4. Carboplatin AUC 5 intravenous infusion in 500ml glucose 5% over 60 minutes
   Administration Instructions
   The dose of carboplatin is capped at a creatinine clearance of 125ml/min. The internationally recommended maximum dose of carboplatin for AUC 5 is 750mg. The national dose bands do not contain this dose so the cap has been set at 790mg in ARIA. Please check this dose is appropriate for your patient

5. Etoposide 100mg/m^2 intravenous infusion in 1000ml sodium chloride 0.9% over 60 minutes

Take Home Medicines

6. Etoposide 200mg/m^2 once a day oral for 2 days starting on day 2 of the chemotherapy cycle
   Administration Instructions
   Oral SACT
   Start on day 2 of the cycle

7. Dexamethasone 4mg twice a day oral for 3 days starting on day 2 of the cycle
Administration Instructions
   Take 4mg twice a day (morning and lunch) for 3 days starting on day two of the cycle

8. Metoclopramide 10mg three times a day when required oral
   Administration Instructions
   Please supply 28 tablets or an original pack as appropriate

9. Ondansetron 8mg twice a day oral for 3 days starting on the evening of day 1 of the cycle
   Administration Instructions
   Take 8mg twice a day for three days starting on the evening of day 1 of the cycle

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.2	August 2022	Carboplatin national dose bands changed Warning added Administration Instructions added to summary	Dr Deborah Wright Pharmacist	Donna Kimber Pharmacy Technician
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.