Chemotherapy Protocol

GYNAECOLOGICAL CANCER

CARBOPLATIN (AUC 2)-PACLITAXEL

(7 day)

Regimen

- Cervix-Carboplatin (AUC 2)-Paclitaxel (7 day)

Indication

- Metastatic cervical cancer
- WHO performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Carboplatin	Thrombocytopenia, peripheral neuropathy, nephrotoxicity at high doses, electrolyte disturbances
Paclitaxel	Hypersensitivity, hypotension, bradycardia, peripheral neuropathy, myalgia and back pain on administration

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

Monitoring

Drugs

- FBC prior to days 1, 8 and 15
- LFTs and U&Es prior to day 1 of each cycle.
- EDTA or calculated creatinine clearance prior to day 1 of each cycle
- CA125 prior to day 1 of each cycle

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities 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.

Haematological

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

Prior to each cycle 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

Day 1

Neutrophils ($x10^9$/L)	**Dose Modifications (carboplatin and paclitaxel)**
1 or greater	100%
less than 1	Delay for 7 days. If the counts recover to $1.5x10^9$/L or more within this time continue with the full dose. If counts do not recover or repeated delays are required then delay until recovery and reduce dose by 20%
Platelets ($x10^9$/L)	**Dose Modifications (carboplatin and paclitaxel)**
100 or greater	100%
less than 100	Delay for 7 days. If the counts recover to $100x10^9$/L or more within this time continue with the full dose. If the counts do not recover or repeated delays are required then delay until recovery and reduce dose by 20%.

Day 8 and 15

Neutrophils ($x10^9$/L)	**Dose Modifications (carboplatin and paclitaxel)**
1 or greater	100%
less than 1	Omit (discuss with consultant)
Platelets ($x10^9$/L)	**Dose Modifications (carboplatin and paclitaxel)**
100 or greater	100%
75 - 100	75% (discuss with consultant)
less than 75	Omit (discuss with consultant)

Hepatic Impairment

Drug	Bilirubin (µmol/L)	Dose
Carboplatin	N/A	No dose adjustment needed
Paclitaxel	51 or greater	Not recommended

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Carboplatin*	less than 20	Omit
Paclitaxel	N/A	No dose adjustment needed

* Significant changes in GFR of more than 10% may require dose adjustment.

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.

For all other non-haematological NCI-CTC grade 3 and above toxicities delay treatment until the adverse effect has resolved to NCI-CTC grade 1 or below. The dose of the causative agent should then be reduced to 75% of the original dose or discontinued as appropriate.

Regimen

21 day cycle for 6 cycles

Drug	Dose	Days	Administration
Carboplatin	AUC 2 (max dose 300mg)	1, 8, 15	Intravenous infusion in 500ml Glucose 5% over 60 minutes
Paclitaxel	80mg/m^2	1, 8, 15	Intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes.

Dose Information

- Carboplatin will be dose banded in accordance with the national dose bands (10mg/ml)
- The recommended maximum dose of carboplatin when using a calculated creatinine clearance at AUC2 is 300mg. If you have an obese patient or an individual with a calculated creatinine clearance above 125ml/min please seek advice from the relevant consultant.

- Paclitaxel will be dose banded in accordance with the national dose bands (6mg/ml)

Administration Information

Extravasation

- Carboplatin – irritant
- Paclitaxel - vesicant

Other

- Hypersensitivity reactions tend to occur with the first or second infusion of paclitaxel. Paclitaxel infusion should be interrupted for minor symptoms such as flushing or localised rashes. If these resolve promptly (within 5 minutes) the infusion may be restarted at a lower rate with intensive monitoring. Immediately discontinue the infusion for severe reactions which include profound hypotension, bronchospasm and generalised erythema.
- Paclitaxel must be administered via a non-PVC administration set containing an in-line 0.22 micron filter.

Additional Therapy

- Premedication to reduce of risk of hypersensitivity reaction

  30 minutes before chemotherapy

  - chlorphenamine 10mg intravenous
  - dexamethasone 10mg oral or intravenous
  - H_2 antagonist according to local formulary choice and availability

- Antiemetics

  15-30 minutes prior to chemotherapy

  - ondansetron 8mg oral or intravenous

  As take home medication

  - dexamethasone 2mg oral daily for 2 days
  - metoclopramide 10mg oral three times a day as required

- 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.

References
1. NICE Guidance TA55 - Guidance on the use of paclitaxel in the treatment of ovarian cancer. Jan 2003
2. NICE Guidance TA91 - Ovarian cancer (advanced) - paclitaxel, pegylated liposomal doxorubicin hydrochloride and topotecan (review). May 2005
3. Safra T, Menczer J, Bernstein R et al. Combined weekly carboplatin and paclitaxel as primary treatment of advanced epithelial ovarian carcinoma; Gynecol.Oncol. 2009;114 (2): 215-218.

REGIMEN SUMMARY

Carboplatin (AUC2)-Paclitaxel (7 day)

Day 1, 8, 15

1. Chlorphenamine 10mg intravenous

2. Dexamethasone 10mg intravenous

3. H_2 antagonist according to local formulary choice and availability
   Administration Instructions:
   Administer according to local formulary choice and availability one of the following 30 minutes prior to SACT;
   - famotidine 20mg oral once only
   - nizatidine 150mg oral once only
   - ranitidine 150mg oral once only
   - ranitidine 50mg intravenous once only

   There are stock shortages of H_2 antagonists. The administration may proceed without these agents being given unless there is a specific instruction from the prescriber in the ARIA journal that a H_2 antagonist must be administered. Many Trusts do not administer an H_2 antagonist from cycle three onwards. They have been left in the ARIA protocols so that decisions can be made on an individual Trust and patient basis.

4. Ondansetron 8mg oral or intravenous
   Administration Instructions
   Administer 15-30 minutes prior to SACT. This may be given as ondansetron 8mg intravenous if required

5. Paclitaxel 80mg/m^2 in 250ml sodium chloride 0.9% intravenous infusion over 60 minutes.

6. Carboplatin AUC 2 (maximum dose 300mg) intravenous infusion in 500ml glucose 5% over 60 minutes.

Take Home Medicines (day 1 only)

7. Metoclopramide 10mg three times a day for 2 days then 10mg three times a day when required for nausea oral
   Administration Instructions
   Please supply 56x10mg tablets or nearest equivalent pack size.

8. Dexamethasone 2mg once a day for 2 days starting on the day after SACT
   Administration Instructions
   Please supply sufficient tablets on day 1 to cover days 1, 8, 15 of the cycle

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.3	Aug 2022	Carboplatin changed to national dose bands	Dr Deborah Wright Pharmacist	Donna Kimber Pharmacy Technician
1.2	October 2020	Update of premedication due to shortage of IV ranitidine. IV ranitidine changed to H_2 antagonist according to local formulary choice and availability Dose banding statement updated Carboplatin maximum dose dded Coding removed	Aram Shortland Pharmacist	Dr Deborah Wright Pharmacist
1.1	March 2014	Bolus removed from “intravenous bolus” Metoclopramide dose changed to 10mg OPCS changed Disclaimer added	Dr Deborah Wright Pharmacist	Donna Kimber Pharmacy Technician
1	May 2013	None	Rebecca Wills Pharmacist Dr Deborah Wright Pharmacist	Dr Clare Green Consultant Medical Oncologist Dr Cheng 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 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.