Chemotherapy Protocol

BREAST CANCER

CARBOPLATIN (AUC 5)-PACLITAXEL(7 day)

Regimen

- Breast-Carboplatin (AUC 5)-Paclitaxel (7 day)

Indication

- Neo-adjuvant treatment of stage II/III triple negative breast cancer
- WHO performance status 0, 1

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

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 or the use of erythropoietin according to NICE TA323 if patient symptomatic of anaemia or has haemoglobin of less than 8g/dL (80g/L)

Day 1

Neutrophils (x10^9/L)	Dose Modifications (carboplatin and paclitaxel)
1 or greater	100%
less than 1	Delay treatment, repeat full blood count at least weekly, until neutrophils recover to 1 or above. • If recovery takes less than 7 days continue with chemotherapy at the same dose. • If recovery takes more than 7 days reduce the dose of carboplatin and paclitaxel to AUC 4 and 60mg/m^2 respectively for the first occurrence or AUC 3.5 and 45mg/m^2 respectively in the event of a second occurrence.
Platelets (x10^9/L)	**Dose Modifications (carboplatin and paclitaxel)**
75 or greater	100%
less than 75	Delay treatment, repeat full blood count at least weekly, until platelets recover to 75 or above. • If recovery takes less than 7 days continue with chemotherapy at the same dose. • If recovery takes more than 7 days reduce the dose of carboplatin and paclitaxel to AUC 4 and 60mg/m^2 respectively for the first occurrence or AUC 3.5 and 45mg/m^2 respectively in the event of a second occurrence.

Day 8 and 15

Neutrophils (x10^9/L)	Dose Modifications (paclitaxel)
1 or greater	100%
less than 1	Omit
Platelets (x10^9/L)	**Dose Modifications (paclitaxel)**
50 or greater	100%
less than 50	Omit

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

*The GFR should be recalculated, or re-measured, due to:

- renal toxicity (serum creatinine greater than 1.5xULN)
- serum creatinine changes of 10% or greater compared to baseline, or last creatinine value used to calculate carboplatin dose (whichever is most recent)

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 4 cycles

The starting dose of carboplatin AUC5 is used with calculated GFR. AUC4 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.

Drug	Dose	Days	Administration
Carboplatin	AUC 5 (max dose)	1	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 maximum dose of carboplatin at AUC 5 is 750mg. 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.

- 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 server 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 paclitaxel

  - 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 (day 1)
  - metoclopramide 10mg oral or intravenous (day 8 & 15)

  As take home medication (day 1 only)

  - dexamethasone 4mg oral twice a day for 3 days starting on day two of the cycle
  - metoclopramide 10mg oral three times a day as required

- Growth factor as per local formulary choice;
  - filgrastim or bioequivalent 30million units once a day on days 3, 4, 5, 10, 11, 12, 17, 18 and 19 of the cycle subcutaneous
  - lenograstim or bioequivalent 33.6million units once a day days 3, 4, 5, 10, 11, 12, 17, 18 and 19 of the cycle subcutaneous

- 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. von Minckwitz G, Schneeweiss A, Loibl S, et al. Neoadjuvant carboplatin in patients with triple-negative and HER2-positive early breast cancer (GeparSixto; GBG 66): a randomised phase 2 trial. Lancet Oncol2014; 15: 747–56
2. Sikov WM, Berry DA, Perou CM, et al. Impact of the Addition of Carboplatin and/or Bevacizumab to Neoadjuvant Once-per-Week Paclitaxel Followed by Dose-Dense Doxorubicin and Cyclophosphamide on Pathologic Complete Response Rates in Stage II to III Triple-Negative Breast Cancer: CALGB 40603 (Alliance). J Clin Oncol. 2015;33(1):13-21.

REGIMEN SUMMARY

Carboplatin (AUC5)-Paclitaxel (weekly)

Day 1

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

   If there is no stock of these products due to national shortages treatment may proceed without the H_2 antagonist provided there is no instruction in the ARIA journal indication the patient **must have** H_2 antagonist treatment.

   All infusion related reactions must be recorded in the ARIA journal and reported to the appropriate consultant. 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 chemotherapy
   This may be given as ondansetron 8mg IV stat if required

5. Paclitaxel 80mg/m^2 in 250ml sodium chloride 0.9% intravenous infusion over 60 minutes.
   Administration Instructions
   Paclitaxel must be administered via a non-PVC administration set containing an in-line 0.22micron filter

6. 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.

7. Carboplatin AUC 5 (max dose) 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

Take Home Medicines (day 1)

8. Metoclopramide 10mg three times a when required for nausea oral
   Administration Instructions
   Please supply 60 tablets or nearest equivalent on day 1 only.

9. Dexamethasone 4mg twice a day for 3 days oral starting on day two of the cycle

10. Growth Factor as directed
    Administration instructions:
    Growth factor as per local formulary choice:
    - filgrastim or bioequivalent 30million units once a day on days 3, 4 , 5, 10, 11, 12, 17, 18, 19 of the cycle subcutaneous
    - lenograstim or bioequivalent 33.6million units once a day days 3, 4, 5, 10, 11, 12, 17, 18, 19 of the cycle subcutaneous

Day 8 & 15

11. Chlorphenamine 10mg intravenous

12. Dexamethasone 10mg intravenous

13. H_2 antagonist according to local formulary choice and availability
    Administration Instructions:
    Administer according to local formulary choice and availability one of the following;
    - ranitidine 50mg intravenous once only
    - famotidine 20mg oral once only
    - Nizatidine 150mg oral once only
    - Ranitidine 150mg oral once only

14. Metoclopramide 10mg oral or intravenous

15. Paclitaxel 80mg/m^2 in 250ml sodium chloride 0.9% intravenous infusion over 60 minutes.
    Administration Instructions
    Paclitaxel must be administered via a non-PVC administration set containing an in-line 0.22 micron filter

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.2	Aug 2022	Anaemia statement updated Carboplatin maximum dose added Carboplatin dose bands added Warning added to summary	Dr Deborah Wright Pharmacist	Donna Kimber Pharmacy Technician
1.1	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 Coding removed	Arum Shortland Pharmacist	Dr Deborah Wright Pharmacist
1	September 2019	None	Rebecca Wills Pharmacist Dr Deborah Wright Pharmacist	Dr J Marshall Consultant Clinical 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.