Chemotherapy Protocol

BREAST CANCER

CARBOPLATIN (AUC6)-DOCETAXEL- PERTUZUMAB-TRASTUZUMAB (IV/SC)

Regimen

- Breast Cancer – Carboplatin (AUC6)-Docetaxel-Pertuzumab-Trastuzumab (IV/SC)

Indication

- Neo-Adjuvant treatment of high risk (node positive or negative tumour greater than or equal to one centimetre) HER2 positive breast cancer that that is locally advanced, inflammatory, or early-stage with a high risk of recurrence, in adults.

- WHO Performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Carboplatin	Neuropathy, nephrotoxicity, ototoxicity, thrombocytopenia
Docetaxel	Hypersensitivity, fluid retention, neuropathy, joint pains, nail changes, fatigue, alopecia, neutropenia
Pertuzumab	Diarrhoea, hypersensitivity reactions, headache, reduced appetite, dyspnoea, cough, vomiting, nausea, constipation, rash, pain, oedema, fatigue, asthenia, cardiotoxicity
Trastuzumab	Cardiotoxicity, acute respiratory distress syndrome, infusion related effects

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

Monitoring

Regimen

- FBC, U&E's and LFT's prior to each cycle

- EDTA or calculated creatinine clearance before the first cycle

- HER2 status prior to initiating therapy

- Cardiac function must be assessed prior to starting treatment. Thereafter, cardiac function should be assessed every 9-12 weeks and as clinically indicated.

- Blood pressure prior to each trastuzumab administration

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. This is especially true in the adjuvant / neoadjuvant setting where dose delays and reductions may be less appropriate. The following is a general guide only.

Haematological

Prior to prescribing the following treatment criteria must be met;

Criteria	Eligible Level
Neutrophils	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 has a haemoglobin of less than 8g/dL (80g/L)

If counts on day one are below these criteria for neutrophil and/or platelets then delay carboplatin and docetaxel treatment for seven days. Only re-start treatment when these levels are reached. If patients experience a febrile neutropenia or a treatment delay due to neutrophil count of less than 0.5 $x10^9$/L or platelets less than 50 $x10^9$/L for more than seven days, then reduce the dose of carboplatin and docetaxel to 80% of the original dose. If the neutropenia or thrombocytopenia recurs despite this decrease in dose intensity, the dose should either be further reduced to 50% of the original dose or treatment stopped.

Haematological dose modifications are not necessary for pertuzumab or trastuzumab. If patients do not tolerate either pertuzumab or trastuzumab, treatment should be stopped. The haematological modifications refer to carboplatin and docetaxel only.

Liver Impairment

Drug	Bilirubin (µmol/L)		AST/ALT (units)		Alk Phos (units)	Dose (% of original dose)
Carboplatin	No dose adjustment needed					
Docetaxel	N/A		1.5xULN or greater	and	2.5xULN or greater	Consider 75%
	Greater than ULN	and/or	3.5xULN or greater	and	6xULN or greater	Not Recommended
Pertuzumab	The safety and efficacy of pertuzumab has not been established in hepatic impairment					
Trastuzumab	No dose adjustment needed					

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Carboplatin	20ml/min or less	Contra-indicated
Docetaxel	No dose adjustment necessary	
Pertuzumab	No dose adjustment necessary in mild to moderate renal impairment. No information in severe renal impairment – clinical decision	
Trastuzumab	No dose adjustment necessary	

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.

Docetaxel

Peripheral neuropathy at NCI-CTC grade 3 should result in a dose reduction from 75mg/m^2 to 60mg/m^2. If the NCI-CTC grade 3 neuropathy occurred at doses lower than 75mg/m^2 or a NCI-CTC grade 4 toxicity develops stop treatment.

Excessive tearing / lacrimation are related to cumulative docetaxel doses and occur after a median of 400mg/m^2. Symptomatic treatment with hypromellose 0.3% eye drops four times a day may help. However, if the ocular irritation continues reduce the docetaxel dose to 60mg/m^2 in the first instance.

Delay the docetaxel where a NCI-CTC grade 3 cutaneous toxicity is present on day one of the cycle until it resolves to NCI-CTC grade 1 or below. The subsequent doses of docetaxel should be reduced to from 75mg/m^2 to 60mg/m^2. If it occurs with a dose of 60mg/m^2 or if there is no recovery after two weeks, docetaxel treatment should be stopped. Where a NCI-CTC grade 3 cutaneous toxicity occurs between

cycles with recovery by day one then reduce the docetaxel dose as described. Docetaxel should be stopped in response to a NCI-CTC grade 4 cutaneous toxicity.

Pertuzumab

The diarrhoea can be severe in patients treated with pertuzumab. It is important to ensure patients are given appropriate therapy for the treatment of diarrhoea. This is not included in the regimen on ARIA and must be added from the support folder.

Pertuzumab and Trastuzumab

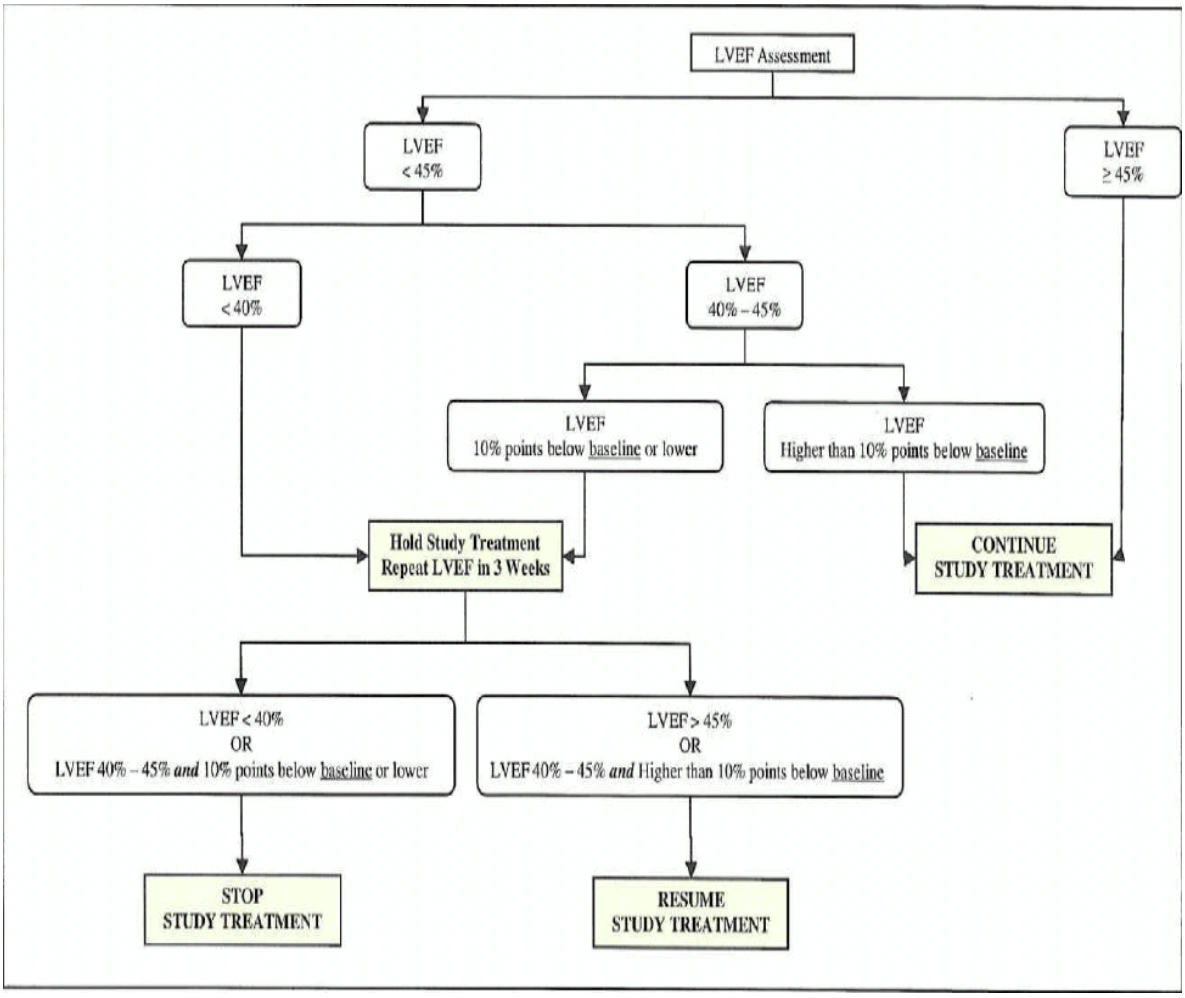
Cardiac

The LVEF should be fifty or above before starting cycle one of pertuzumab and trastuzumab.

Subsequent Echocardiograms

The flow chart below describes the process to be followed if there is an asymptomatic decline in LVEF during pertuzumab and trastuzumab treatment. This is taken from the study protocol as used in the reference section. Study treatment refers to pertuzumab and trastuzumab.

The LVEF should be fifty or above before starting cycle one of trastuzumab.



In general patients who develop **symptomatic** cardiac dysfunction should have pertuzumab and trastuzumab discontinued, be commenced on ACE inhibitor therapy and be referred to a cardiologist. Further treatment should be discussed with the relevant oncology consultant..

Regimen

The starting dose of carboplatin AUC6 is used with calculated GFR. AUC 5 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 AUC 6 is 900mg. 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.

Docetaxel is highly myelosuppressive and in those with poor bone marrow reserves (for example due to extensive prior treatment, bone metastasis or extensive skeletal radiation) consider a starting dose of 55mg/m² with a view to increase to 75mg/m² if well tolerated.

21 day cycle for 6 cycles. Trastuzumab is then continued post surgery as monotherapy for a further 12 cycles (18 cycles of treatment in total)

Cycle 1

Drug	Dose	Days	Administration
Carboplatin	AUC 6 (max dose)	2	Intravenous infusion in 500ml glucose 5% over 60 minutes
Docetaxel	75mg/m^2	2	Intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes
Pertuzumab	840mg	1	Intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes
Trastuzumab	8mg/kg	1	Intravenous infusion in 250ml sodium chloride 0.9% over 90 minutes

Cycle 2, 3, 4, 5, 6

Drug	Dose	Days	Administration
Carboplatin	AUC 6 (max dose)	1	Intravenous infusion in 500ml glucose 5% over 60 minutes
Docetaxel	75mg/m^2	1	Intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes
Pertuzumab	420mg	1	Intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes
Trastuzumab	6mg/kg	1	Intravenous infusion in 250ml sodium chloride 0.9% over 90 minutes

Cycle 7 – 18 (12 cycles will be set in ARIA)

Drug	Dose	Days	Administration
Trastuzumab	600mg	1	Subcutaneous injection over 3 – 5 minutes

Dose Information

- Carboplatin will be dose banded in accordance with the national dose bands (10mg/ml)
- The maximum dose of carboplatin for AUC 6 is 900mg. This will be set as 890mg in ARIA to comply with the national bands
- Docetaxel will be dose banded according to the national dose bands (20mg/ml)
- Docetaxel induced fluid retention can lead to weight gain. This is not a reason to alter the doses

- If the time between two sequential infusions of pertuzumab is less than six weeks, the 420mg dose should be administered as soon as possible without regard to the next planned dose. If the time between two sequential infusions is 6 weeks or more, the initial loading dose of 840mg should be re-administered as a 60 minute intravenous infusion followed every 3 weeks thereafter by a maintenance dose of 420 mg administered over a period of 30 to 60 minutes.

- Intravenous trastuzumab will be dose banded in accordance with national dose bands (21mg/ml trastuzumab)

- If the patient misses a dose of intravenous trastuzumab by seven days or less, then the usual maintenance dose of 6mg/kg should be given as soon as possible. Do not wait until the next planned cycle. Subsequent maintenance doses should be given according to the previous schedule

- If the patient misses a dose of intravenous trastuzumab by more than seven days, a re-loading dose of 8mg/kg should be given over 90 minutes. Subsequent maintenance doses should then be given every 21 days from that point

- If the patient misses a dose of subcutaneous trastuzumab it is recommended to administer the 600mg dose as soon as possible. The interval between consecutive subcutaneous administrations should not be less than three weeks.

Administration Information

- Hypersensitivity reactions tend to occur with the first or second infusion of docetaxel. The docetaxel infusion should not be interrupted for minor symptoms such as flushing or localised rashes. Immediately discontinue the infusion for severe reactions which include profound hypotension, bronchospasm and generalised erythema.

- Docetaxel doses of more than 200mg should be diluted in 500ml sodium chloride 0.9% (maximum concentration 0.74mg/ml)

- Pertuzumab has been associated with hypersensitivity and infusion related reactions. Patients should be observed for 60 minutes after the first infusion and for 30 minutes after the second infusion, provided no reaction occurred on the first infusion. If patients have tolerated the first two infusions with no infusion related reactions consideration can be given to eliminating this observation period.

- Intravenous trastuzumab is associated with hypersensitivity reactions. Patients should be observed for six hours following the start of the first infusion of trastuzumab and for two hours following the start of the second infusion. If the patient has tolerated the first two infusions with no infusion related effects consideration can be given to eliminating this observation period.

- The first infusion of intravenous trastuzumab must be administered over 90 minutes. If this is well tolerated administer subsequent infusions over 30 minutes

- The injection site of the subcutaneous trastuzumab should be alternated between the left and right thigh. New injections should be given at least 2.5cm from the old site and never into areas where the skin is red, bruised, tender or hard

Extravasation

- Carboplatin - irritant
- Docetaxel – vesicant
- Pertuzumab - neutral
- Trastuzumab (intravenous) – neutral

Additional Therapy

- Antiemetics

  15-30 minutes before chemotherapy

  - ondansetron 8mg oral or intravenous

  As take home medication

  - metoclopramide 10mg three times a day when required oral
  - ondansetron 8mg twice a day for three days oral

- To prevent fluid retention and hypersensitivity reactions prescribe dexamethasone 8mg twice a day oral for three days starting 24 hours before the docetaxel administration. On the occasions where individuals attend for treatment and have forgotten to take the dexamethasone pre-medication administer dexamethasone 20mg once only dose intravenous bolus.

- Diarrhoea is a common adverse effect, particularly on cycle one. Consider prescribing loperamide 4mg after the first loose motion then 2mg after each loose motion thereafter. This is included on cycle one only and can be added from the support folder thereafter

- For treatment of pertuzumab or trastuzumab infusion reactions ‘once only when required’ doses of the following should be prescribed;

  - chlorphenamine 10mg intravenous
  - hydrocortisone 100mg intravenous
  - paracetamol 1000mg oral

- Growth factors according to local formulary choice. For example:

  - filgrastim or bioequivalent 30million units once a day for 7 days starting from day 3 subcutaneous
  - lenograstim or bioequivalent 33.6million units once a day for 7 days starting from day 3 subcutaneous

- pegfilgrastim or bioequivalent 6mg once only on day 2 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.Valero V, Forbes J, Pegram MD et al. Multicentre phase III randomised trial comparing docetaxel and trastuzumab with docetaxel, carboplatin and trastuzumab as first line chemotherapy for patients with HER2 positive gene amplified metastatic breast cancer (BCIRG007 study); two highly active therapeutic regimens. J Clin Oncol 2011; 29 (2): 149-156.
2.Baselga J, Cortes J, Sung-Bae K et al. Peruzumab plus trastuzumab plus docetaxel for metastatic breast cancer. N Engl J Med 2012; 366 (2): 109-11

REGIMEN SUMMARY

Carboplatin (AUC6)-Docetaxel-Pertuzumab-Trastuzumab (IV/SC)

Cycle 1

Day One

1. Dexamethasone 8mg twice a day oral (from TTO)*
   Administration Instructions
   Ensure the patient has taken the dexamethasone pre-medication the day before and the day of docetaxel administration (and the day after). On the occasions where individuals attend for treatment and have forgotten to take the dexamethasone pre-medication administer dexamethasone 20mg (or equivalent dose) IV stat 15-30 minutes before chemotherapy. If the patient has already taken a dose of dexamethasone do not administer this dose

2. Pertuzumab 840mg intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes
   Administration Instructions
   The first infusion of pertuzumab should be given over 60 minutes. If this is well tolerated subsequent infusions may be given over 30 minutes

3. Trastuzumab 8mg/kg intravenous infusion in 250ml sodium chloride 0.9% over 90 minutes
   Administration Instructions
   The first infusion of trastuzumab must be administered over 90 minutes. If this is well tolerated administer subsequent infusions over 30 minutes

4. Chlorphenamine 10mg intravenous when required for infusion related reactions

5. Hydrocortisone 100mg intravenous when required for infusion related reactions

6. Paracetamol 1000mg oral when required for infusion related reactions
   Administration Instructions
   Please check if the patient has taken paracetamol. Maximum dose is 4g per 24 hours. There should be 4 hours between doses

Day Two

7. Dexamethasone 8mg twice a day oral (from TTO)*
   Administration Instructions
   Ensure the patient has taken the dexamethasone pre-medication the day before and the day of docetaxel administration (and the day after). On the occasions where individuals attend for treatment and have forgotten to take the dexamethasone pre-medication administer dexamethasone 20mg (or equivalent dose) IV stat 15-30 minutes before chemotherapy. If the patient has already taken a dose of dexamethasone do not administer this dose

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

9. Docetaxel 75mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes
   Administration Instructions
   Ensure the patient has taken the dexamethasone pre-medication the day before and the day of docetaxel administration (and the day after). On the occasions where individuals attend for treatment and have forgotten to take the dexamethasone pre-medication administer dexamethasone 20mg (or equivalent dose) IV stat 15-30 minutes before chemotherapy. If the patient has already taken a dose of dexamethasone do not administer this dose

10. Carboplatin AUC6 intravenous infusion in 500ml glucose 5% over 60 minutes
    Administration Instructions
    This recommended maximum dose is 900mg based on a creatinine clearance of 125ml/min. This will be set at 890mg in ARIA to comply with national dose bands

Take Home Medicines (given on day 1)

11. Dexamethasone 8mg twice a day oral for 3 days starting the day before the docetaxel infusion.
    Administration Instructions
    This is the supply for the next cycle. Take in the morning and at lunchtime

12. Metoclopramide 10mg three times a day when required oral
    Administration Instructions
    Please supply 28x10mg tablets or nearest equivalent pack size

13. Ondansetron 8mg twice a day for 3 days starting on the evening of the day of chemotherapy (not antibody) administration oral
    Administration Instructions
    Start on the evening of the day of chemotherapy (not antibody administration)

14. Loperamide 4mg after the first loose stool and 2mg after each subsequent loose stool to a maximum of 16mg in 24 hours
    Administration Instructions
    Take 4mg after the first loose stool and then 2mg after each subsequent loose stool to a maximum of 16mg in 24 hours. Please supply one original pack size

15. Growth factor according to local formulary choice
    Administration Instructions
    Growth factors according to local formulary choice. For example;
    - filgrastim or bioequivalent 30million units once a day for 7 days starting from day 3 subcutaneous
    - lenograstim or bioequivalent 33.6million units once a day for 7 days starting from day 3 subcutaneous
    - pegfilgrastim or bioequivalent 6mg once only on day 2 subcutaneous

Cycles 2, 3, 4, 5

Day One

16. Pertuzumab 420mg intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes
    Administration Instructions
    The first infusion of pertuzumab should be given over 60 minutes. If this is well tolerated subsequent infusions may be given over 30 minutes

17. Trastuzumab 6mg/kg intravenous infusion in 250ml sodium chloride 0.9% over 90 minutes
    Administration Instructions
    The first infusion of trastuzumab must be administered over 90 minutes. If this is well tolerated administer subsequent infusions over 30 minutes

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

19. Docetaxel 75mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes
    Administration Instructions
    Ensure the patient has taken the dexamethasone pre-medication the day before and the day of docetaxel administration (and the day after). On the occasions where individuals attend for treatment and have forgotten to take the dexamethasone pre-medication administer dexamethasone 20mg (or equivalent dose) IV stat 15-30 minutes before chemotherapy. If the patient has already taken a dose of dexamethasone do not administer this dose

20. Carboplatin AUC 6 intravenous infusion in 500ml glucose 5% over 60 minutes
    Administration Instructions
    This recommended maximum dose is 900mg based on a creatinine clearance of 125ml/min. This will be set at 890mg in ARIA to comply with national dose bands

21. Chlorphenamine 10mg intravenous when required for infusion related reactions

22. Hydrocortisone 100mg intravenous when required for infusion related reactions

23. Paracetamol 1000mg oral when required for infusion related reactions
    Administration Instructions
    Please check if the patient has taken paracetamol. Maximum dose is 4g per 24 hours. There should be 4 hours between doses

Take Home Medicines

24. Dexamethasone 8mg twice a day oral for 3 days starting the day before the docetaxel infusion.
    Administration Instructions
    This is the supply for the next cycle. Take in the morning and lunchtime

25. Metoclopramide 10mg three times a day when required oral
    Administration Instructions
    Please supply 28x10mg tablets or nearest equivalent pack size

26. Ondansetron 8mg twice a day for 3 days starting on the evening of the day of chemotherapy (not antibody) administration oral
    Administration Instructions
    Start on the evening of the day of chemotherapy (not antibody administration)

27. Growth factor according to local formulary choice
    Administration Instructions
    Growth factors according to local formulary choice. For example;
    - filgrastim or bioequivalent 30million units once a day for 7 days starting from day 3 subcutaneous
    - lenograstim or bioequivalent 33.6million units once a day for 7 days starting from day 3 subcutaneous
    - pegfilgrastim or bioequivalent 6mg once only on day 2 subcutaneous

Cycle 6

Day One

28. Pertuzumab 420mg intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes
    Administration Instructions
    The first infusion of pertuzumab should be given over 60 minutes. If this is well tolerated subsequent infusions may be given over 30 minutes

29. Trastuzumab 6mg/kg intravenous infusion in 250ml sodium chloride 0.9% over 90 minutes
    Administration Instructions
    The first infusion of trastuzumab must be administered over 90 minutes. If this is well tolerated administer subsequent infusions over 30 minutes

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

31. Docetaxel 75mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes
    Administration Instructions
    Ensure the patient has taken the dexamethasone pre-medication the day before and the day of docetaxel administration (and the day after). On the occasions where individuals attend for treatment and have forgotten to take the dexamethasone pre-medication administer dexamethasone 20mg (or equivalent dose) IV stat 15-30 minutes before chemotherapy. If the patient has already taken a dose of dexamethasone do not administer this dose

32. Carboplatin AUC6 intravenous infusion in 500ml glucose 5% over 60 minutes
    Administration Instructions
    This recommended maximum dose is 900mg based on a creatinine clearance of 125ml/min. This will be set at 890mg in ARIA to comply with national dose bands

33. Chlorphenamine 10mg intravenous when required for infusion related reactions

34. Hydrocortisone 100mg intravenous when required for infusion related reactions

35. Paracetamol 1000mg oral when required for infusion related reactions
    Administration Instructions
    Please check if the patient has taken paracetamol. Maximum dose is 4g per 24 hours. There should be 4 hours between doses

Take Home Medicines

36. Metoclopramide 10mg three times a day when required oral
    Administration Instructions
    Please supply 28x10mg tablets or nearest equivalent pack size

37. Ondansetron 8mg twice a day for 3 days starting on the evening of the day of chemotherapy (not antibody) administration oral
    Administration Instructions
    Start on the evening of the day of chemotherapy (not antibody administration)

38. Growth factor according to local formulary choice
    Administration Instructions
    Growth factors according to local formulary choice. For example;
    - filgrastim or bioequivalent 30million units once a day for 7 days starting from day 3 subcutaneous
    - lenograstim or bioequivalent 33.6million units once a day for 7 days starting from day 3 subcutaneous
    - pegfilgrastim or bioequivalent 6mg once only on day 2 subcutaneous

Cycle 7 – 18

Day One

39. Trastuzumab 600mg subcutaneous injection over 3 – 5 minutes
    Administration Instructions
    The injection site of the subcutaneous trastuzumab should be alternated between the left and right thigh. New injections should be given at least 2.5cm from the old site and never into areas where the skin is red, bruised, tender or hard.

40. Chlorphenamine 10mg intravenous when required for infusion related reactions

41. Hydrocortisone 100mg intravenous when required for infusion related reactions

42. Paracetamol 1000mg oral when required for infusion related reactions
    Administration Instructions
    Please check if the patient has taken paracetamol. Maximum dose is 4g per 24 hours. There should be 4 hours between doses

*Cycle one dexamethasone must be prescribed in advance of the chemotherapy. In Aria Planner the dexamethasone 8mg twice daily will appear on days 1, 2, 3 of treatment. This is the supply for the next cycle. The administration instructions reflect this. On the last cycle no dexamethasone will appear for prescribing.

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.3	Sept 2024	Trastuzumab national dose banding added	Alexandra Pritchard Pharmacist	Nanda Basker Pharmacist
1.2	Aug 2022	Carboplatin national dose band and maximum dose. Coding removed Admin instructions added in summary	Dr Deborah Wright Pharmacist	Donna Kimber Pharmacy Technician
1.1	April 2019	Trastuzumab missed doses changed to seven days Pertuzumab and trastuzumab observation period reduced on second and subsequent infusions Docetaxel extravasation changed to vesicant Ondansetron added to antiemetic regimen Loperamide added to TTO Growth factors added to TTO Paracetamol administration instructions added Carboplatin maximum dose added Disclaimer updated	Dr Deborah Wright Pharmacist	Rebecca Wills Pharmacist
1	July 2017	None	Nanda Basker Pharmacist	Dr Sanjay Raj 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 Hospitals 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 that occur as a result of following these guidelines. These protocols should be used in conjunction with other references such as the Summary of Product Characteristics and relevant published papers