Breast–Cyclophosphamide-Epirubicin-Paclitaxel-Pertuzumab-Trastuzumab (EC-PPH)

Regimen

- Breast Cancer – Cyclophosphamide-Epirubicin-Paclitaxel-Pertuzumab-Trastuzumab (EC-PPH)

Indication

- Neo-adjuvant / adjuvant therapy of breast cancer
- WHO Performance status 0, 1, 2

Toxicity

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adverse Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>Dysuria, haemorrhagic cystitis, taste disturbances</td>
</tr>
<tr>
<td>Epirubicin</td>
<td>Cardio-toxicity, urinary discolouration (red)</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>Hypersensitivity, hypotension, bradycardia, peripheral neuropathy, myalgia and</td>
</tr>
<tr>
<td></td>
<td>back pain on administration</td>
</tr>
<tr>
<td>Pertuzumab</td>
<td>Diarrhea, hypersensitivity reactions, headache, reduced appetite, dyspnoea,</td>
</tr>
<tr>
<td></td>
<td>cough, vomiting, nausea, constipation, rash, pain, oedema, fatigue, asthenia,</td>
</tr>
<tr>
<td></td>
<td>cardiotoxicity</td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>Cardio toxicity, acute respiratory distress syndrome, infusion related effects</td>
</tr>
</tbody>
</table>

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

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.

Monitoring

Regimen

- FBC, U&E’s and LFT’s prior to day 1 for cycles containing cyclophosphamide, epirubicin and paclitaxel. A full blood count should also be conducted before days 8 and 15 of paclitaxel administration. During the administration of trastuzumab with pertuzumab alone this may be reduced to once every three months.
- Ensure adequate cardiac function before and at regular intervals during treatment. Baseline LVEF should be measured, particularly in patients with a history of cardiac problems or in the elderly. An echocardiogram should be
conducted before cycle four and then three monthly thereafter.

- HER2 status before initiating therapy

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. The following guidelines apply to chemotherapy only.

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.

Haematological

Prior to prescribing the following treatment criteria must be met on day 1 of treatment.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Eligible Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophils</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>

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL (80g/l).

In the adjuvant / neo-adjuvant setting always check with the relevant consultant before delaying or reducing the dose in response to a toxicity.

If counts on day one are below these criteria for neutrophils and platelets then delay treatment for seven days. Treatment should only be re-started when these levels are reached. Treatment may be resumed at the original dose or reduce the dose of cyclophosphamide and epirubicin to 80% of the original dose where a NCI-CTC grade 3 or above haematological event has occurred. Consider stopping the paclitaxel. If a second episode of neutropenia and / or thrombocytopenia occurs, despite dose reduction or the time to reach the eligible level is longer than seven days consider changing or stopping therapy.

No dose modifications for haematological toxicity are necessary for pertuzumab or trastuzumab. If treatment is not tolerated it should be stopped.
### Kidney Impairment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Creatinine Clearance (ml/min)</th>
<th>Dose (% of original dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>more than 20</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>10-20</td>
<td>75</td>
</tr>
<tr>
<td></td>
<td>Less than 10</td>
<td>50</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>No dose adjustment necessary</td>
<td></td>
</tr>
<tr>
<td>Epirubicin</td>
<td>Dose reduce in severe impairment only</td>
<td></td>
</tr>
<tr>
<td>Pertuzumab</td>
<td>The safety and efficacy of pertuzumab has not been established in renal impairment</td>
<td></td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>No dose adjustment necessary</td>
<td></td>
</tr>
</tbody>
</table>

### Liver Impairment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>Dose reduction may not be necessary</td>
</tr>
<tr>
<td>Epirubicin</td>
<td><strong>Bilirubin (umol/L)</strong></td>
</tr>
<tr>
<td></td>
<td>24-51</td>
</tr>
<tr>
<td></td>
<td>52-85</td>
</tr>
<tr>
<td></td>
<td>85 or greater</td>
</tr>
<tr>
<td></td>
<td>If AST 2-4 x ULN and bilirubin 21-51μmol/L give 50% dose , if the AST greater than 4 x ULN or bilirubin greater than 51μmol/L then give 25% dose</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td><strong>less than 26</strong></td>
</tr>
<tr>
<td></td>
<td>27-51</td>
</tr>
<tr>
<td></td>
<td>greater than 51</td>
</tr>
<tr>
<td></td>
<td>If bilirubin less than 1.25xULN and transaminase less than 10xULN then prescribe the last dose otherwise consider a dose reduction or stopping treatment.</td>
</tr>
<tr>
<td>Pertuzumab</td>
<td>The safety and efficacy of pertuzumab has not been established in hepatic impairment</td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>No dose adjustment necessary</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.
**Epirubicin**

Discontinue epirubicin if cardiac failure develops.

**Paclitaxel**

NCI-CTC grade 2 peripheral neuropathy withhold paclitaxel only until the neuropathy recovers to NCI-CTC grade 1 then dose reduce to 75% of the original dose. Where the peripheral neuropathy is NCI-CTC grade 3 again withhold the paclitaxel until it resolves to NCI-CTC grade 1 and then reduce the dose of paclitaxel to 50% of the original dose. Paclitaxel should be discontinued if the neuropathy does not resolve to NCI-CTC grade 1.

**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.
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

Cyclophosphamide-Epirubicin (EC)

21 day cycle for 4 cycles (cycles 1, 2, 3, 4)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Days</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>500mg/m²</td>
<td>1</td>
<td>Intravenous bolus</td>
</tr>
<tr>
<td>Epirubicin</td>
<td>90mg/m²</td>
<td>1</td>
<td>Intravenous bolus</td>
</tr>
</tbody>
</table>

Followed by;

Paclitaxel-Pertuzumab-Trastuzumab

21 day cycle for 4 cycles

Cycle 5

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Days</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paclitaxel</td>
<td>80mg/m²</td>
<td>1, 8, 15</td>
<td>Intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes</td>
</tr>
<tr>
<td>Pertuzumab</td>
<td>840mg</td>
<td>1</td>
<td>Intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes</td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>8mg/kg</td>
<td>1</td>
<td>Intravenous infusion in 250ml sodium chloride 0.9% over 90 minutes</td>
</tr>
</tbody>
</table>

Followed by;

Cycle 6, 7, 8

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Days</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paclitaxel</td>
<td>80mg/m²</td>
<td>1, 8, 15</td>
<td>Intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes</td>
</tr>
<tr>
<td>Pertuzumab</td>
<td>420mg</td>
<td>1</td>
<td>Intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes</td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>6mg/kg</td>
<td>1</td>
<td>Intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes</td>
</tr>
</tbody>
</table>

Cycles 9-22 inclusive

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Days</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pertuzumab</td>
<td>420mg</td>
<td>1</td>
<td>Intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes</td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>6mg/kg</td>
<td>1</td>
<td>Intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes</td>
</tr>
</tbody>
</table>
Dose Information

- Cyclophosphamide will be dose banded in accordance with the national dose bands (20PM).
- Epirubicin will be dose banded in accordance with the national dose bands (2PM).
- The maximum lifetime cumulative dose of epirubicin is 900mg/m².
- Paclitaxel will be dosed banded in accordance with the national dose bands (6mg/mL).
- 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.
- Trastuzumab will be dose rounded to the nearest 50mg (up if halfway).
- If the patient misses a dose of 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 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.

Administration Information

- Hypersensitivity reactions tend to occur with the first or second infusion of paclitaxel. Paclitaxel infusions 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.
- Pertuzumab has been associated with hypersensitivity and infusion related reactions. Patients should be observed for 60 minutes after the first infusion and for 30 – 60 minutes after subsequent infusions. If patients have tolerated the first two infusions with no infusion related reactions consideration can be given to reducing this observation period.
- Trastuzumab is associated with hypersensitivity reactions. The SPC recommends patients should be observed for six hours following the start of the first infusion of trastuzumab and for two hours following the start of
subsequent infusions. In practice these times have been reduced. If the patient has tolerated the first two infusions with no infusion related effects consideration can be given to reducing or stopping this observation period.

Extravasation

- Cyclophosphamide – neutral
- Epirubicin – vesicant
- Paclitaxel - vesicant
- Pertuzumab – neutral
- Trastuzumab - neutral

Additional Therapy

- **EC**
  
  EC antiemetics day 1
  
  15-30 minutes prior to chemotherapy;
  
  - aprepitant 125mg oral
  - dexamethasone 4mg oral or intravenous
  - ondansetron 8mg oral or intravenous

  As take home medication
  
  - aprepitant 80mg once a day for 2 days
  - dexamethasone 2mg twice a day for 3 days oral
  - metoclopramide 10mg three times a day when required oral
  - ondansetron 8mg twice a day for 3 days oral

  Growth factor according to local formulary choice. For example;

  - filgrastim or bioequivalent 30 million units once a day subcutaneous for five days starting on day five of the cycle
  - lenograstim or bioequivalent 33.6 million units once a day subcutaneous for five days starting on day five of the cycle
  - pegfilgrastim or bioequivalent 6mg once a day subcutaneous on day two of the cycle

- Paclitaxel
  
  15-30 minutes prior to chemotherapy with **paclitaxel**
  
  - metoclopramide 10mg oral or intravenous

  As take home medication
  
  - metoclopramide 10mg three times a day when required oral
• Premedication to reduce of risk of paclitaxel hypersensitivity reaction

  30 minutes prior to chemotherapy with paclitaxel
  - chlorphenamine 10mg intravenous
  - dexamethasone 10mg intravenous
  - H₂ antagonist according to local formulary choice and availability

• 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 once oral

• Mouthwashes according to local or national policy on the treatment of mucositis

• Gastric protection with a proton pump inhibitor or a H₂ antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

References
2. Ramshorst M, van der Voot A, van Werkhoven E et al. Neoadjuvant chemotherapy with or without anthracyclines in the presence of dual HER2 blockade for HER2-positive breast cancer (TRAIN-2): a multicentre, open-label, randomised, phase 3 trial. Lancet Oncology 2018: 19 (12); 1630-1640
REGIMEN SUMMARY

Cyclophosphamide-Epirubicin-Paclitaxel-Pertuzumab-Trastuzumab (EC-PPH)

Cycle 1, 2, 3, 4

1. Aprepitant 125mg oral
2. Dexamethasone 4mg oral or intravenous
3. Ondansetron 8mg oral or intravenous
4. Epirubicin 90mg/m² intravenous bolus over 10 minutes
5. Cyclophosphamide 500mg/m² intravenous bolus over 10 minutes

Take Home Medicines

6. Aprepitant 80mg once a day oral for 2 days starting on day 2 of the cycle
   Administration Instructions
   Take 80mg once a day for 2 days starting on day 2 of the cycle

7. Dexamethasone 2mg twice a day for 3 days oral starting on day two of the cycle
   Administration Instructions
   Take 2mg 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
   When required for nausea. Please supply five days or an original pack if appropriate.

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

10. Growth factor according to local formulary choice.
    Administration Instructions
    Dispense according to local formulary choices;
    - filgrastim or bioequivalent 30 million units once a day subcutaneous for 5 days starting on day 5 of the cycle
    - lenograstim or bioequivalent 33.6million units once a day subcutaneous for 5 days starting on day 5 of the cycle
    - pegfilgrastim or bioequivalent 6mg once a day subcutaneous on day 2 of the cycle

Paclitaxel-Pertuzumab-Trastuzumab

Cycle 5

Day 1

11. 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
12. 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.

13. Chlorphenamine 10mg intravenous

14. Dexamethasone 10mg intravenous

15. H₂ 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 chemotherapy:
   - ranitidine 50mg intravenous once only
   - famotidine 20mg oral once only
   - nizatidine 150mg oral once only
   - ranitidine 150mg oral once only

   If there is no stock of these products due to national shortages treatment may proceed without the H₂ antagonist provided there is no instruction in the ARIA journal indication the patient must have H₂ 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 H₂ 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.

16. Metoclopramide 10mg oral or intravenous

17. Paclitaxel 80mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes

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

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

20. 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 8, 15

1. Chlorphenamine 10mg intravenous

2. Dexamethasone 10mg intravenous

3. H₂ antagonist according to formulary choice and availability.
   Administration Instructions:
   Administer according to local formulary choice and availability one of the following 30 minutes prior to chemotherapy:
   - ranitidine 50mg intravenous once only
   - famotidine 20mg oral once only
   - nizatidine 150mg oral once only
   - ranitidine 150mg oral once only

   If there is no stock of these products due to national shortages treatment may proceed without the H₂ antagonist provided there is no instruction in the ARIA journal indication the patient must have H₂ 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 H₂ 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. Metoclopramide 10mg oral or intravenous

5. Paclitaxel 80mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes
   Administration Instructions
   Paclitaxel must be administered via a non-PVC administration set containing an in-line 0.22 micron filter

**Take Home Medicines (Day 1 only)**

21. Metoclopramide 10mg three times a day when required oral

22. 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

**Cycle 6, 7, 8**

**Day 1**

23. 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

24. 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

25. Chlorphenamine 10mg intravenous

26. Dexamethasone 10mg intravenous

27. H₂ antagonists 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 chemotherapy;
   - ranitidine 50mg intravenous once only
   - famotidine 20mg oral once only
   - nizatidine 150mg oral once only
   - ranitidine 150mg oral once only

   If there is no stock of these products due to national shortages treatment may proceed without the H₂ antagonist provided there is no instruction in the ARIA journal indication the patient must have H₂ 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 H₂ 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.

28. Metoclopramide 10mg oral or intravenous

29. Paclitaxel 80mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 60 minutes
30. Chlorphenamine 10mg intravenous when required for infusion related reactions

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

32. 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 8, 15

32. Chlorphenamine 10mg intravenous

33. Dexamethasone 10mg intravenous

34. H\textsubscript{2} antagonist according to formulary choice and availability.
   Administration Instructions
   Administer according to local formulary choice and availability one of the following 30 minutes prior to chemotherapy:
   - ranitidine 50mg intravenous once only
   - famotidine 20mg oral once only
   - nizatidine 150mg oral once only
   - ranitidine 150mg oral once only

   If there is no stock of these products due to national shortages treatment may proceed without the H\textsubscript{2} antagonist provided there is no instruction in the ARIA journal indicating the patient must have H\textsubscript{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\textsubscript{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.

35. Metoclopramide 10mg oral or intravenous

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

Take Home Medicines (Day 1 only)

37. Metoclopramide 10mg three times a day when required oral

Cycles 9 – 22

Day 1

33. 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

34. 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
35. Chlorphenamine 10mg intravenous when required for infusion related reactions

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

37. 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.
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.