Network
Chemotherapy Protocols
Breast Cancer
Notes from the editor

These protocols are available on the Network website www.tvcn.nhs.uk.

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Acknowledgements
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Network Chemotherapy Protocols
Breast Cancer

Network Chemotherapy Protocols used in the management of Breast cancer.
Date published: March 2012
Date of review: March 2014

Chemotherapy Protocols

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<td>Paclitaxel Carboplatin</td>
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<td>Trastuzumab 8/6 (21 day)</td>
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List of amendments in this version

Protocol type: Breast Tumours
Date due for review: March 2014
Previous Version number: 3.1
This version number: 3.2

Table 1 Amendments

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<th>Page</th>
<th>Action Type</th>
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<td>P65</td>
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Table 2 New protocols to be approved and checked by TSSG included in this version

<table>
<thead>
<tr>
<th>Name of protocol</th>
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<th>Reason / Proposer</th>
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</tbody>
</table>

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**AC (60/600)**

*Indication: Adjuvant*

**DRUG REGIMEN**

**Day 1**  
**CYCLOPHOSPHAMIDE** 600mg/m² IV bolus  
**DOxorubicin** 60mg/m² IV bolus

*Cycle Frequency: Every 21 days for 4 cycles*

**DOSE MODIFICATIONS**

**Doxorubicin**

Dose reduce in severe renal impairment.

- Bilirubin 20-50micromol/L give 50% dose
- Bilirubin 51-85micromol/L give 25% dose
- Bilirubin >85micromol/L omit
- If ALT/AST is 2-3 x ULN give 75% dose
- If ALT/AST is >3 x ULN give 50% dose

Maximum cumulative dose = 450-550mg/m² (in normal cardiac function)  
= 400mg/m² (in patients with cardiac dysfunction or exposed to mediastinal irradiation)

**Cyclophosphamide**

- GFR >50ml/min give 100% dose
- GFR 10-50ml/min give 75% dose
- GFR <10ml/min give 50% dose

**INVESTIGATIONS**

Routine Blood test

1) Blood results required before chemotherapy administration

<table>
<thead>
<tr>
<th>Give</th>
<th>Discuss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL ≥10</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>Plt x 10⁹/L ≥100</td>
<td>&lt; 100</td>
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<tr>
<td>Neutrophils x 10⁹/L ≥1.5</td>
<td>&lt; 1.5</td>
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</tbody>
</table>

2) Non urgent blood tests

Tests relating to disease response/progression

3) ECG (possible ECHO) required if patient has preexisting cardiac disease (Doxorubicin)
CONCURRENT MEDICATION

ANTIEMETIC POLICY
Highly emetogenic

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Cardiotoxicity – monitor cardiac function. Doxorubicin may be stopped in future cycles if signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue. Cyclophosphamide may irritate bladder, drink copious volumes of water.
CMF IV (21 day)

Indication: Advanced or recurrent disease.
Adjuvant treatment for frail patients who are unlikely to tolerate other regimens

DRUG REGIMEN

Day 1  CYCLOPHOSPHAMIDE 600mg/m² IV bolus
       METHOTREXATE 40mg/m² IV bolus
       5FLUOROURACIL 600mg/m² IV bolus

Cycle Frequency: Every 21 days for 6 cycles

DOSE MODIFICATIONS

Previous neutropenic sepsis, discuss with Consultant or Registrar
Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant.

Methotrexate
GFR 45 - 60 mL/min give 65% dose
GFR 30 - 45 mL/min give 50% dose
GFR <30 mL/min omit dose

Bilirubin 53 - 85 micromol/L or ALT/AST >180 give 75% dose
Bilirubin >85 micromol/L omit

Fluorouracil
GFR <30 ml/min give 80% dose
Bilirubin 50-85 micromol/L give 50% dose
Bilirubin >85 micromol/L or ALT/AST >180 omit

Palmar plantar (handfoot syndrome) treat with pyridoxine and if symptoms fail to improve then consider reducing the dose of 5FU

Cyclophosphamide
GFR >50ml/min give 100% dose
GFR 10-50ml/min give 75% dose
GFR <10ml/min give 50% dose
INVESTIGATIONS
Routine Blood test
1) Blood results required before chemotherapy administration

<table>
<thead>
<tr>
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<th>Give</th>
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<tr>
<td>Hb x g/dL</td>
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<td>&lt; 10</td>
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<td>Neutrophils x 10^9/L</td>
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<tr>
<td>Plt x 10^9/L</td>
<td>≥1.5</td>
<td>&lt; 1.5</td>
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</tbody>
</table>

2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION
Calcium folinate (calcium leucovorin) 15mg PO/IV every 6 hours for 6 doses starting 24 hours after Methotrexate if:
- Pleural effusions/ascites
- Previous mucositis
- Serum creatinine > 120micromols/L

ANTIEMETIC POLICY
Moderately emetogenic.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (handfoot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouthcare
Diarrhoea – treat with codeine or loperamide
Methotrexate induced mucositis - folinic acid (calcium folinate) rescue (see concurrent medication)
Cyclophosphamide may irritate bladder, drink copious volumes of water.
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease, arrhythmias or angina pectoris or those who develop chest pain during treatment with fluorouracil
CMF IV CLASSICAL (28 day)

Indication: High risk adjuvant breast

**DRUG REGIMEN**

**Day 1**  
*CYCLOPHOSPHAMIDE* 600mg/m² IV bolus  
METHOTREXATE 40mg/m² IV bolus  
FLUOROURACIL 600mg/m² IV bolus

**Day 8**  
*CYCLOPHOSPHAMIDE* 600mg/m² IV bolus  
METHOTREXATE 40mg/m² IV bolus  
FLUOROURACIL 600mg/m² IV bolus

*N.B.* an alternative exists using oral Cyclophosphamide (see separate protocol)

**Cycle Frequency: Every 28 days for 6 cycles**

**DOSE MODIFICATIONS**

Previous neutropenic sepsis, discuss with Consultant or Registrar  
Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant.

**Methotrexate**

GFR 45 - 60 mL/min give 65% dose  
GFR 30 - 45 mL/min give 50% dose  
GFR <30mL/min omit dose  
Bilirubin 53 - 85micromol/L or ALT//AST >180 give 75% dose  
Bilirubin >85 micromol/L omit

**Fluorouracil**

GFR <30mL/min give 80% dose  
Bilirubin 50-85 micromol/L give 50% dose  
Bilirubin >85micromol/L or ALT/AST >180 omit

Palmar plantar (handfoot syndrome) treat with pyridoxine and if symptoms fail to improve then consider reducing the dose of 5FU

**Cyclophosphamide**

GFR >50ml/min give 100% dose  
GFR 10-50ml/min give 75% dose  
GFR <10ml/min give 50% dose
INVESTIGATIONS
Routine Blood test 1) Blood results required before chemotherapy administration

<table>
<thead>
<tr>
<th>Test</th>
<th>Level 1</th>
<th>Level 2</th>
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<td>Hb g/dL</td>
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2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION
Calcium folinate (calcium leucovorin) 15mg PO/IV every 6 hours for 6 doses starting 24 hours after Methotrexate if:
- Pleural effusions/ascites
- Previous mucositis
- Serum creatinine > 120micromols/L

ANTIEMETIC POLICY
Moderately emetogenic days 1, 8

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
- Palmar plantar (handfoot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
- Mucositis – use routine mouthcare
- Diarrhoea – treat with codeine or loperamide
- Methotrexate induced mucositis - folinic acid (calcium folinate) rescue (see concurrent medication)
- Cyclophosphamide may irritate bladder, drink copious volumes of water.
- Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease, arrhythmias or angina pectoris or those who develop chest pain during treatment with fluorouracil.
CMF PO CLASSICAL (28 day)

Indication: High risk adjuvant breast

DRUG REGIMEN
Day 1  CYCLOPHOSPHAMIDE* 100mg/m² PO for 14 days
   METHOTREXATE 40mg/m² IV bolus
   FLUOROURACIL 600mg/m² IV bolus
Day 8  METHOTREXATE 40mg/m² IV bolus
   FLUOROURACIL 600mg/m² IV bolus

*N.B. an alternative exists using IV cyclophosphamide day 1 and 8 (see separate protocol)

Cycle Frequency: Every 28 days for 6 cycles

DOSE MODIFICATIONS
Previous neutropenic sepsis, discuss with Consultant or Registrar
Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant.

Methotrexate
GFR 45 - 60mL/min give 65% dose
GFR 30 - 45mL/min give 50% dose
GFR <30mL/min omit dose
Bilirubin 53 - 85micromol/L or ALT//AST > 180 give 75% dose
Bilirubin >85micromol/L omit

Fluorouracil
GFR <30mL/min give 80% dose
Bilirubin 50-85micromol/L give 50% dose
Bilirubin >85micromol/L or ALT/AST >180 omit

Palmar plantar (handfoot syndrome) treat with pyridoxine and if symptoms fail to improve then consider reducing the dose of 5FU

Cyclophosphamide
GFR >50ml/min give 100% dose
GFR 10-50ml/min give 75% dose
GFR <10ml/min give 50% dose
INVESTIGATIONS
Routine Blood test 1) Blood results required before chemotherapy administration

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2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION
Calcium folinate (calcium leucovorin) 15mg PO/IV every 6 hours for 6 doses starting 24 hours after Methotrexate if:
- Pleural effusions/ascites
- Previous mucositis
- Serum creatinine > 120micromols/L

ANTIEMETIC POLICY
Moderately emetogenic days 1, 8

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (handfoot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouthcare
Diarrhoea – treat with codeine or loperamide
Methotrexate induced mucositis - folinic acid (calcium folinate) rescue (see concurrent medication)
Cyclophosphamide may irritate bladder, drink copious volumes of water.
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease, arrhythmias or angina pectoris or those who develop chest pain during treatment with fluorouracil.
**EC**

*Indication: Adjuvant*

**DRUG REGIMEN**

*Day 1*  
**CYCLOPHOSPHAMIDE** 600mg/m² IV bolus  
**EPIRUBICIN** 75mg/m² IV bolus

*Cycle Frequency: Every 21 days for 4 cycles*

**DOSE MODIFICATIONS**

**Epirubicin**
- Bilirubin 20-50 micromol/L give 50% dose  
- Bilirubin 51-85 micromol/L give 25% dose  
- Bilirubin >85 micromol/L omit  
Dose reduce in severe renal impairment.  
Maximum lifetime dose = 1000mg/m² (with normal cardiac function)  
= 650mg/m² (in patients with cardiac dysfunction or exposed to mediastinal irradiation)

**Cyclophosphamide**
- GFR >50ml/min give 100% dose  
- GFR 10-50ml/min give 75% dose  
- GFR <10ml/min give 50% dose

**INVESTIGATIONS**

Routine Blood test  
1) Blood results required before chemotherapy administration  
   *Give Discuss*
   - Hb x g/dL ≥10 < 10  
   - Plt x 10⁹/L ≥100 < 100  
   - Neutrophils x 10⁹/L ≥1.5 < 1.5

2) Non urgent blood tests  
Tests relating to disease response/progression

3) ECG (possible ECHO) required if patient has preexisting cardiac disease (Epirubicin)
CONCURRENT MEDICATION

ANTIEMETIC POLICY
Highly emetogenic

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Cardiotoxicity – monitor cardiac function. Epirubicin may be stopped in future cycles if signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue.
Cyclophosphamide may irritate bladder, drink copious volumes of water.
**Indication: Adjuvant treatment of early breast cancer. May be given with concurrent RT.**

NICE guidance - www.nice.org.uk

Trastuzumab for the adjuvant treatment of early-stage HER2-positive breast cancer: Trastuzumab, given at 3-week intervals for 1 year or until disease recurrence (whichever is the shorter period) is recommended as a treatment option for early stage HER2 positive breast cancer following surgery, chemotherapy (neoadjuvant or adjuvant) and radiotherapy (if applicable). In keeping with NICE guidance, patients must have received (neo)adjuvant chemotherapy and have adequate cardiac function.

**DRUG REGIMEN**

**Cycle 1 only**

**Day 1 Loading dose** (to be given day 1 cycle 1 only)

*TRASTUZUMAB 8mg/kg in 250ml sodium chloride 0.9% infusion over 90 minutes*

**Cycles 2 to 18**

**Day 1 Maintenance dose**

TRASTUZUMAB 6mg/kg in 250ml sodium chloride 0.9% infusion over 30** or 90 minutes

*NB. Patients need to remain on the ward / day unit for monitoring for 6 hours post first dose*

**Cycle Frequency: Loading dose once only followed by 17 maintenance doses 3 weekly (unless reloading required following a break in treatment) (18 cycles in total)**

**DOSE MODIFICATIONS**

No dose reduction or cessation of Trastuzumab is required if patient has acute reversible neutropenia

Refer to TVCN adjuvant Trastuzumab guidelines
If trastuzumab infusion is delayed by more than 7 days the patient should be reloaded at 8mg/kg.

Continuation and discontinuation of trastuzumab based on interval LVEF assessment

- If LVEF <44 hold trastuzumab, repeat LVEF in 3 weeks.
  - If repeat LVEF <44 or LVEF 45-49 and >10 points from baseline then stop trastuzumab.
  - If repeat LVEF 45-49 and <10 points from baseline or LVEF >49 resume trastuzumab.

- If LVEF 45-49 and >10 EF points from baseline hold trastuzumab, repeat LVEF in 3 weeks.
  - If repeat LVEF <44 or LVEF 45-49 and >10 points from baseline stop trastuzumab.
  - If repeat LVEF 45-49 and <10 points from baseline or LVEF >49 resume trastuzumab.

- If LVEF > 50 or LVEF 45-49 and <10 EF points from baseline continue trastuzumab.

New LVEF assessment results should be available by the day of the next scheduled trastuzumab administration and a decision to give or hold the dose must be made based on this algorithm.
INVESTIGATIONS
Routine Blood test
1) Blood results required 3 monthly

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<tr>
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- U&Es & LFTs
- Baseline weight and 3 monthly weight.
- Monitor cardiac function (ECG/ECHO/MUGA) of all patients baseline and at 3, 6, 9, 12 months during treatment and at 6, 12 and 24 months following cessation after treatment.

2) Tests relating to disease response/progression

CONCURRENT MEDICATION
Trastuzumab infusion related chills and/or fevers – treat with paracetamol and chlorphenamine.

ANTIEMETIC POLICY
Minimal emetogenic risk.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Cardiotoxicity – monitor cardiac function.
Trastuzumab infusion related chills and/or fevers are commonly observed during the first infusion (but infrequently with subsequent infusions). Other symptoms may include nausea, hypertension, vomiting, pain, rigors, headache, cough, dizziness, rash, and asthenia.
Some adverse reactions to trastuzumab infusion including dyspnoea, hypotension, wheezing, bronchospasm, supraventricular tachyarrhythmia, reduced oxygen saturation and respiratory distress can be serious and potentially fatal.
If symptoms of back ache, nausea or vomiting, do a set of obs. Give hydrocortisone 100mg IV, chlorphenamine 10mg IV.

REFERENCE
FEC 60

_Indication: Metastatic breast cancer_

**DRUG REGIMEN**

**Day 1**

- **FLUOROURACIL** 600mg/m² IV bolus
- **EPIRUBICIN** 60mg/m² IV bolus
- **CYCLOPHOSPHAMIDE** 600mg/m² IV bolus

**Cycle Frequency:** Every 21 days for 6 cycles (4 cycles if unable to cope/tolerate)

**DOSE MODIFICATIONS**

Previous neutropenic sepsis, Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant

**Epirubicin**

- Bilirubin 20-50micromol/L give 50% dose
- Bilirubin 51-85micromol/L give 25% dose
- Bilirubin >85micromol/L omit

Dose reduce in severe renal impairment.

Maximum lifetime dose = 650mg/m² (in patients with cardiac dysfunction or exposed to mediastinal irradiation) = 1000mg/m² (with normal cardiac function)

**Fluorouracil**

- GFR <30ml/min give 80% dose
- Bilirubin 50-85micromol/L give 50% dose
- Bilirubin >85micromol/L or ALT/AST >180 omit

**Cyclophosphamide**

- GFR >50ml/min give 100% dose
- GFR 10-50ml/min give 75% dose
- GFR <10ml/min give 50% dose

**INVESTIGATIONS**

Routine Blood test

1) Blood results required before chemotherapy administration

<table>
<thead>
<tr>
<th></th>
<th>Give</th>
<th>Discuss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL</td>
<td>≥10</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>Plt x 10⁹/L</td>
<td>≥100</td>
<td>&lt; 100</td>
</tr>
<tr>
<td>Neutrophils x 10⁹/L</td>
<td>≥1.5</td>
<td>0.75-1.0 (on the day of chemo go ahead with GCSF support as per local policy, no chemo dose reductions). &lt;0.75 wait until neutrophils ≥ 0.75.</td>
</tr>
</tbody>
</table>

FEC 60

Breast TSSG Chair Authorisation:

Review: March 2014

Version 3.2

Network Chemotherapy Protocols – Breast Cancer 18 of 83
2) Non urgent blood tests
   - Tests relating to disease response/progression
   - ECG (possible ECHO) required if patient has preexisting cardiac disease (Epirubicin)

CONCURRENT MEDICATION

ANTIEMETIC POLICY
Highly emetogenic

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouthcare
Diarrhoea – treat with codeine or loperamide
Cardiotoxicity – monitor cardiac function. Epirubicin may be stopped in future cycles if signs of
cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue.
Cyclophosphamide may irritate bladder, drink copious volumes of water.
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease,
arrhythmias or angina pectoris or those who develop chest pain during treatment with fluorouracil.
**FEC 75/600**

**Indication:** Neoadjuvant / adjuvant and metastatic breast cancer

**DRUG REGIMEN**

Day 1  
**FLUOROURACIL** 600mg/m² IV bolus  
**EPIRUBICIN** 75mg/m² IV bolus  
**CYCLOPHOSPHAMIDE** 600mg/m² IV bolus

GCSF as per local policy

**Cycle Frequency:** Every 21 days for 6 cycles (review after 4 cycles)

**DOSE MODIFICATIONS**

Previous neutropenic sepsis, Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant

**Epirubicin**

- Bilirubin 20-50micromol/L give 50% dose  
- Bilirubin 51-85micromol/L give 25% dose  
- Bilirubin >85micromol/L omit  

Dose reduce in severe renal impairment.

Maximum lifetime dose  = 650mg/m² (in patients with cardiac dysfunction or exposed to mediastinal irradiation)  
= 1000mg/m² (with normal cardiac function)

**Fluorouracil**

- GFR <30ml/min give 80% dose  
- Bilirubin 50-85micromol/L give 50% dose  
- Bilirubin > 85micromol/L or ALT/AST >180 omit

**Cyclophosphamide**

- GFR >50ml/min give 100% dose  
- GFR 10-50ml/min give 75% dose  
- GFR <10ml/min give 50% dose
INVESTIGATIONS
Routine Blood test
1) Blood results required before chemotherapy administration
   \[
   \begin{align*}
   \text{Hb} & \geq 10 < 10 \\
   \text{Plt} & \geq 100 < 100 \\
   \text{Neutrophils} & \geq 1.5 \\
   \text{0.8-1.5 (on the day of chemo go ahead with GCSF support as per local policy for 7 days starting 48 hours after chemotherapy, no chemo dose reductions).} \\
   <0.8 & \text{wait until neutrophils } \geq 0.8.
   \end{align*}
   \]

2) Non urgent blood tests
   - Tests relating to disease response/progression
   - ECG (possible ECHO) required if patient has preexisting cardiac disease (Epirubicin)

CONCURRENT MEDICATION
Patients who have had previous neutropenic sepsis should go ahead without dose reduction but with prophylactic GCSF support as per local policy (discuss with Consultant).

ANTIEMETIC POLICY
Highly emetogenic

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouthcare
Diarrhoea – treat with codeine or loperamide
Cardiotoxicity – monitor cardiac function. Epirubicin may be stopped in future cycles if signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue.
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease, arrhythmias or angina pectoris or those who develop chest pain during treatment with fluorouracil. Cyclophosphamide may irritate bladder, drink copious volumes of water.

REFERENCES
2. Breast Cancer Adjuvant chemotherapy update, October 07 Dr B A Lavery. TVCN Breast TSSG Lead
FEC 75/500

**Indication:** Neoadjuvant / adjuvant and metastatic breast cancer

**DRUG REGIMEN**
Day 1  
**FLUOROURACIL** 500mg/m² IV bolus  
**EPIRUBICIN** 75mg/m² IV bolus  
**CYCLOPHOSPHAMIDE** 500mg/m² IV bolus  
GCSF as per local policy

*Cycle Frequency: Every 21 days for 6 cycles (review after 4 cycles)*

**DOSE MODIFICATIONS**
Previous neutropenic sepsis, Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant

**Epirubicin**
- Bilirubin 20-50micromol/L give 50% dose
- Bilirubin 51-85micromol/L give 25% dose
- Bilirubin >85micromol/L omit
Dose reduce in severe renal impairment.
Maximum lifetime dose = 650mg/m² (in patients with cardiac dysfunction or exposed to mediastinal irradiation)

= 1000mg/m² (with normal cardiac function)

**Fluorouracil**
- GFR <30ml/min give 80% dose
- Bilirubin 50-85micromol/L give 50% dose
- Bilirubin > 85micromol/L or ALT/AST >180 omit

**Cyclophosphamide**
- GFR >50ml/min give 100% dose
- GFR 10-50ml/min give 75% dose
- GFR <10ml/min give 50% dose
INVESTIGATIONS
Routine Blood test
1) Blood results required before chemotherapy administration

<table>
<thead>
<tr>
<th>Test</th>
<th>Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL</td>
<td>≥10 &lt; 10</td>
</tr>
<tr>
<td>Plt x 10^9/L</td>
<td>≥100 &lt; 100</td>
</tr>
<tr>
<td>Neutrophils x 10^9/L</td>
<td>0.8-1.5</td>
</tr>
</tbody>
</table>

Give Discuss

- 0.8-1.5 (on the day of chemo go ahead with GCSF support as per local policy for 7 days starting 48 hours after chemotherapy, no chemo dose reductions).
- <0.8 wait until neutrophils ≥ 0.8.

2) Non urgent blood tests
- Tests relating to disease response/progression
- ECG (possible ECHO) required if patient has preexisting cardiac disease (Epirubicin)

CONCURRENT MEDICATION
Patients who have had previous neutropenic sepsis should go ahead without dose reduction but with prophylactic GCSF support as per local policy (discuss with Consultant).

ANTIEMETIC POLICY
Moderately emetogenic

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouthcare
Diarrhoea – treat with codeine or loperamide
Cardiotoxicity – monitor cardiac function. Epirubicin may be stopped in future cycles if signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue.
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease, arrhythmias or angina pectoris or those who develop chest pain during treatment with fluorouracil.
Cyclophosphamide may irritate bladder, drink copious volumes of water.

REFERENCES
2. Breast Cancer Adjuvant chemotherapy update, October 07 DrB A Lavery. TVCN Breast TSSG Lead
FEC 100

Indication: Neoadjuvant / adjuvant

DRUG REGIMEN
Day 1 FLUOROURACIL 500mg/m² IV bolus
EPIRUBICIN 100mg/m² IV bolus
CYCLOPHOSPHAMIDE 500mg/m² IV bolus

Cycle Frequency: Every 21 days for 6 cycles (4 cycles if unable to cope)
Neoadjuvant / adjuvant 3 cycles of FEC 100 followed by 3 of Docetaxel
(100mg/m²) see separate protocol.

DOSE MODIFICATIONS
Previous neutropenic sepsis, Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant

Epirubicin
Bilirubin 20-50micromol/L give 50% dose
Bilirubin 51-85micromol/L give 25% dose
Bilirubin >85micromol/L omit
Dose reduce in severe renal impairment.
Maximum lifetime dose = 650mg/m² (in patients with cardiac dysfunction or exposed to mediastinal irradiation)
= 1000mg/m² (with normal cardiac function)

Fluorouracil
GFR <30ml/min give 80% dose
Bilirubin 50-85micromol/L give 50% dose
Bilirubin >85micromol/L or ALT/AST >180 omit

Cyclophosphamide
GFR >50ml/min give 100% dose
GFR 10-50ml/min give 75% dose
GFR <10ml/min give 50% dose
INVESTIGATIONS
Routine Blood test
1) Blood results required before chemotherapy administration
   \[ \begin{array}{lcl}
   \text{Give} & \text{Discuss} \\
   \text{Hb x g/dL} & \geq 10 & < 10 \\
   \text{Plt x } 10^9/L & \geq 100 & < 100 \\
   \text{Neutrophils x } 10^9/L & \geq 1.5 & > 1.5 \text{ (on the day of chemo go ahead with GCSF support as per local policy, no chemo dose reductions).} \\
   \end{array} \]

2) Non urgent blood tests
   - Tests relating to disease response/progression
   - ECG (possible ECHO) required if patient has preexisting cardiac disease (Epirubicin)

CONCURRENT MEDICATION
Patients who have had previous neutropenic sepsis should go ahead without dose reduction but with prophylactic GCSF support as per local policy (discuss with Consultant).

ANTIEMETIC POLICY
Highly emetogenic

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (handfoot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Mucositis – use routine mouthcare
Diarrhoea – treat with codeine or loperamide
Cardiotoxicity – monitor cardiac function. Epirubicin may be stopped in future cycles if signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue.
Cardiotoxicity - special attention is advisable in treating patients with a history of heart disease, arrhythmias or angina pectoris or those who develop chest pain during treatment with fluorouracil. Cyclophosphamide may irritate bladder, drink copious volumes of water.

REFERENCES
1. Sequential Adjuvant Epirubicin-based and Docetaxel Chemotherapy for Node positive Breast Cancer Patients: The FNCLCC PACS 01 Trial. JCO 2006; 24: 5664-5671
2. Breast Cancer Adjuvant chemotherapy update, October 07 Dr B A Lavery. TVCN Breast TSSG Lead
**Indication:** Neoadjuvant breast cancer and adjuvant node positive good performance status <= 65 years breast cancer

**DRUG REGIMEN**

**Day 1**  
FLUOROURACIL 500mg/m² IV bolus  
EPIRUBICIN 100mg/m² IV bolus  
CYCLOPHOSPHAMIDE 500mg/m² IV bolus

**Cycle Frequency:** Every 21 days for 3 cycles followed by

**Day 1**  
PREMEDICATION: DEXAMETHASONE 8mg BD starting 24 hours before chemotherapy (or 20mg IV on day of chemotherapy) and 8mg bd post-chemotherapy for 2 days (for patients who are unable to tolerate high doses of steroids 4mg doses may be considered).  
(This can reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions)  
DOCETAXEL 100mg/m² in 250ml glucose 5% or sodium chloride 0.9% infusion over 1 hour  
Routine GCSF as per local policy

**Cycle Frequency:** Every 21 days for 3 cycles

Clinicians and Nurses may review alternate cycles.

**DOSE MODIFICATIONS**

**Epirubicin**  
Bilirubin 20-50micromol/L give 50% dose  
Bilirubin 51-85micromol/L give 25% dose  
Bilirubin >85micromol/L omit  
Dose reduce in severe renal impairment.  
Maximum lifetime dose = 650mg/m² (in patients with cardiac dysfunction or exposed to mediastinal irradiation)  
= 1000mg/m² (with normal cardiac function)

**Fluorouracil**  
GFR <30ml/min give 80% dose  
Bilirubin 50-85micromol/L give 50% dose  
Bilirubin >85micromol/L or ALT/AST >180 omit

**Cyclophosphamide**  
GFR >50ml/min give 100% dose  
GFR 10-50ml/min give 75% dose  
GFR <10ml/min give 50% dose
**Docetaxel**
Discuss if severe cutaneous reactions, peripheral neuropathy or fluid retention after previous course.

**Hepatic impairment:**
Patients who have both elevations of transaminases (ALT and/or AST) > 1.5 x ULN and ALP > 2.5 x ULN: recommended dose is 75mg/m².
Patients with serum bilirubin > ULN and/or ALT and AST > 3.5 x ULN associated with ALP > 6 x ULN: docetaxel should not be used unless strictly indicated.

**INVESTIGATIONS**
**Routine Blood test**
1) Blood results required before chemotherapy administration
   - **Give**
   - **Discuss**
   - Hb x g/dL \(\geq 10 \ < 10\)
   - Plt x 10⁹/L \(\geq 100 \ < 100\)
   - Neutrophils x 10⁹/L \(\geq 1.5 \ < 1.5\) (on the day of chemo go ahead with GCSF support), as per local policy no dose reductions

2) Non urgent blood tests
Tests relating to disease response/progression

3) ECG (possible ECHO) required if patient has preexisting cardiac disease (Epirubicin)

**CONCURRENT MEDICATION**
Ensure pre-medication is given before docetaxel

**ANTIEMETIC POLICY**
FEC - Highly emetogenic
Docetaxel – Low emetogenic risk

**ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS**
Mucositis – see dose modifications
Diarrhoea – see dose modifications
Cardiotoxicity – monitor cardiac function. Epirubicin may be stopped in future cycles if signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue. Cyclophosphamide may irritate bladder, drink copious volumes of water.
FEC 75 / DOCETAXEL

**Indication:** Neoadjuvant breast cancer and adjuvant node positive good performance status <= 65 years breast cancer

**DRUG REGIMEN**

Day 1  FLUOROURACIL* 500mg/m² IV bolus  
   EPIRUBICIN 75mg/m² IV bolus  
   CYCLOPHOSPHAMIDE* 500mg/m² IV bolus  

* In some Trusts the Fluorouracil and cyclophosphamide doses are 600mg/m²  

**Cycle Frequency:** Every 21 days for 4 cycles followed by  

Day 1  PREMEDICATION: DEXAMETHASONE 8mg BD starting 24 hours before chemotherapy (or 20mg IV on day of chemotherapy) and 8mg bd post-chemotherapy for 2 days (for patients who are unable to tolerate high doses of steroids 4mg doses may be considered).  
   (This can reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions)  
   DOCETAXEL 100mg/m² in 250ml glucose 5% or sodium chloride 0.9% infusion over 1 hour  
   Routine GCSF as per local policy  

**Cycle Frequency:** Every 21 days for 4 cycles  

Clinicians and Nurses may review alternate cycles.  

**DOSE MODIFICATIONS**  

**Epirubicin**  
   Bilirubin 20-50micromol/L give 50% dose  
   Bilirubin 51-85micromol/L give 25% dose  
   Bilirubin >85micromol/L omit  
   Dose reduce in severe renal impairment  
   Maximum lifetime dose = 650mg/m² (in patients with cardiac dysfunction or exposed to mediastinal irradiation)  
   = 1000mg/m² (with normal cardiac function)  

**Fluorouracil**  
   GFR <30ml/min give 80% dose  
   Bilirubin 50-85micromol/L give 50% dose  
   Bilirubin >85micromol/L or ALT/AST >180 omit
**Cyclophosphamide**
GFR >50ml/min give 100% dose
GFR 10-50ml/min give 75% dose
GFR <10ml/min give 50% dose

**Docetaxel**
Discuss if severe cutaneous reactions, peripheral neuropathy or fluid retention after previous course.

Hepatic impairment:
Patients who have both elevations of transaminases (ALT and/or AST) > 1.5 x ULN and ALP > 2.5 x ULN: recommended dose is 75mg/m².
Patients with serum bilirubin > ULN and/or ALT and AST > 3.5 x ULN associated with ALP > 6 x ULN: docetaxel should not be used unless strictly indicated.

**INVESTIGATIONS**
Routine Blood test
1) Blood results required before chemotherapy administration

<table>
<thead>
<tr>
<th>Test</th>
<th>Required range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL</td>
<td>≥10 &lt; 10</td>
</tr>
<tr>
<td>Plt x 10⁹/L</td>
<td>≥100 &lt; 100</td>
</tr>
<tr>
<td>Neutrophils x 10⁹/L</td>
<td>≥1.5 &lt; 1.5</td>
</tr>
</tbody>
</table>

(on the day of chemo go ahead with GCSF support), as per local policy no dose reductions

2) Non urgent blood tests

Tests relating to disease response/progression

3) ECG (possible ECHO) required if patient has preexisting cardiac disease (Epirubicin)

**CONCURRENT MEDICATION**
Ensure pre-medication is given before docetaxel

**ANTIEMETIC POLICY**
FEC - Highly emetogenic
Docetaxel – Low emetogenic risk

**ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS**
Mucositis – see dose modifications
Diarrhoea – see dose modifications
Cardiotoxicity – monitor cardiac function. Epirubicin may be stopped in future cycles if signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, and tachycardia with fatigue.
Cyclophosphamide may irritate bladder, drink copious volumes of water.
DOCETAXEL 100 adjuvant (21 day)

**Indication:** Neoadjuvant / adjuvant

*First line adjuvant use in cases where anthracyclines cannot be used (previous anthracyclines for a previous breast cancer, serious cardiac problems etc),*

NICE guidance approved the use of Docetaxel in the adjuvant setting for node positive women. NICE guidance named TAC as the regime to use, but this has substantial toxicity risks, and high rates of neutropenic sepsis. UK breast groups have opted for the TACT trial regime instead. The French results are the best in the literature, and after consideration at the TVCN Breast TSSG it is recommended that the PACS01 schedule is used when an adjuvant taxane based regime is recommended for node positive cases.

**DRUG REGIMEN**

**Day 1**

PREMEDICATION: DEXAMETHASONE 8mg BD starting 24 hours before chemotherapy (or 20mg IV on day of chemotherapy) and 8mg bd post-chemotherapy for 2 days (for patients who are unable to tolerate high doses of steroids 4mg doses may be considered).

(This can reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions)

**DOCETAXEL** 100mg/m² in 250ml sodium chloride 0.9% infusion over 1 hour

**Cycle Frequency:** Every 21 days

*3 cycles when following 3 cycles of FEC 100(see separate protocol)*

**DOSE MODIFICATIONS**

Discuss if severe cutaneous reactions, peripheral neuropathy or fluid retention after previous course.

Hepatic impairment: Patients who have both elevations of transaminases (ALT and/or AST) > 1.5xULN and ALP > 2.5 x ULN: recommended SPC dose is 75 mg/m².

Patients with serum bilirubin > ULN and/or ALT and AST > 3.5 x ULN associated with ALP > 6 x ULN: docetaxel should not be used unless strictly indicated.

**INVESTIGATIONS**

Routine Blood test

1) Blood results required before chemotherapy administration

<table>
<thead>
<tr>
<th></th>
<th>Give</th>
<th>Discuss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL</td>
<td>≥10</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>Plt x 10⁹/L</td>
<td>≥100</td>
<td>&lt; 100</td>
</tr>
<tr>
<td>Neutrophils x 10⁹/L</td>
<td>≥1.5</td>
<td>&lt; 1.5</td>
</tr>
</tbody>
</table>

2) Non urgent blood tests.

Tests relating to disease response/progression

CONCURRENT MEDICATION
Ensure premedication given. This can reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions.

ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Discuss if severe cutaneous reactions, peripheral neuropathy or fluid retention after previous course.

REFERENCES
1. Breast Cancer Adjuvant chemotherapy update, October 07 Dr B A Lavery. TVCN Breast TSSG Lead
3. Sequential Adjuvant Epirubicin-based and Docetaxel Chemotherapy for Node positive Breast Cancer Patients: The FNCLCC PACS 01 Trial. JCO 2006; 24: 5664-5671
4. Epirubicin increases long term survival in adjuvant chemotherapy of patients with poor prognosis, node-positive, early breast cancer: 10 year follow up results of the French Adjuvant Study Group 05 Randomized Trial. JCO 2005; 23: 2686-2693
5. NICE technology appraisal guidance 109 September 2006
Thames Valley Cancer Network

CAPECITABINE 1000 MONOTHERAPY (1000mg/m² BD)

Indication: First line monotherapy of metastatic advanced breast cancer

NICE guidance – www.nice.org.uk
Capecitabine monotherapy is recommended as an option for people with locally advanced or metastatic breast cancer who have not previously received capecitabine in combination therapy and for whom anthracycline and taxane containing regimens have failed or further anthracycline treatment is contraindicated.

DRUG REGIMEN
Days 1 to 14 1000mg/m² twice daily (2000mg/m²/day) po for 14 days followed by a 7 day rest

NB the lower starting dose above is used in breast and heavily pretreated patients it may be increasing if tolerated to the licensed dose of 1250mg/m² twice daily (2500mg/m²/day) po.

‘However 50% of the patients in the main phase 3 trial required a reduction of capecitabine dose. This dose reduction was not associated with any increased risk of progression or resistance to treatment, in fact there was slightly better controlled disease in those whose dose reduced by 25% in the oral Capecitabine arm (the above dose)’

NB Tablets available as strengths of 150mg and 500mg.

Cycle Frequency: Every 21 days for 6 cycles subject to tolerance and response

DOSE MODIFICATIONS
Capecitabine:
Check CrCl prior to every cycle
CrCl (ml/min) >50 give 100% dose
   30 - 50 give 75% dose
   <30 contraindicated

Hepatic impairment – SPC recommends interruption of capecitabine therapy if treatment related elevations in bilirubin of > 3 x ULN or ALT/AST > 2.5 x ULN occur.
Treatment may be resumed when bilirubin decreases to < 3 x ULN or hepatic aminotransferases decrease to < 2.5 x ULN.
Please refer to summary of product characteristics for detailed guidance on dose modifications due to toxicity (including plantar-palmar erythema and gastrointestinal toxicity).
Toxicity can be managed by symptomatic treatment and/or modification of the dose (treatment interruption or dose reduction). Once the dose has been reduced it should not be increased at a later time. Dose limiting toxicities include diarrhoea, abdominal pain, nausea, stomatitis and handfoot syndrome.

### Toxicity Grades

<table>
<thead>
<tr>
<th>Toxicity Grades</th>
<th>Dose changes within a treatment cycle</th>
<th>Dose adjustment for next cycle/dose (% of starting dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Grade 1</td>
<td>Maintain dose level</td>
<td>Maintain dose level</td>
</tr>
<tr>
<td>* Grade 2</td>
<td>- 1st appearance Interrupt until resolved to grade 0-1</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>- 2nd appearance Interrupt until resolved to grade 0-1</td>
<td>75%</td>
</tr>
</tbody>
</table>

### INVESTIGATIONS

**Routine Blood test**

1. Blood results required before chemotherapy administration
   
<table>
<thead>
<tr>
<th>Test</th>
<th>Give</th>
<th>Discuss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL</td>
<td>≥10</td>
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<tr>
<td>Plt x 10^9/L</td>
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<td>&lt; 100</td>
</tr>
<tr>
<td>Neutrophils x 10^9/L</td>
<td>≥1.5</td>
<td>&lt; 1.5</td>
</tr>
</tbody>
</table>

Serum creatinine - GFR should be calculated or measured using EDTA

### CONCURRENT MEDICATION

Patients taking phenytoin concomitantly with capecitabine should be regularly monitored for increased phenytoin plasma concentrations.

Capecitabine enhances the anticoagulant effects of warfarin. Patients taking warfarin concomitantly with capecitabine must have regular monitoring of INR.

### ANTIEMETIC POLICY

Low emetogenic risk

### ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

- Palmar plantar (handfoot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
- Diarrhoea – treat with loperamide or codeine
CAPECITABINE 2000mg bd (7 days on / 7 days off)

**Indication:** Monotherapy of metastatic advanced breast cancer

**NICE guidance – www.nice.org.uk**
Capecitabine monotherapy is recommended as an option for people with locally advanced or metastatic breast cancer who have not previously received capecitabine in combination therapy and for whom anthracycline and taxane containing regimens have failed or are contraindicated.

**DRUG REGIMEN**

| Days 1 to 7 | 2000mg twice daily po for 7 days followed by a 7 day rest |
| Days 15 to 21 | 2000mg twice daily po for 7 days followed by a 7 day rest |

**NB** Tablets available as strengths of 150mg and 500mg.

**Cycle Frequency:** Every 28 days

**DOSE MODIFICATIONS**

**Capecitabine:**
Check CrCl prior to every cycle
- CrCl (ml/min) >50 give 100% dose
- 30 - 50 give 75% dose
- <30 contraindicated

Hepatic impairment – SPC recommends interruption of capecitabine therapy if treatment related elevations in bilirubin of > 3 x ULN or ALT/AST > 2.5 x ULN occur. Treatment may be resumed when bilirubin decreases to < 3 x ULN or hepatic aminotransferases decrease to < 2.5 x ULN.

Please refer to summary of product characteristics for detailed guidance on dose modifications due to toxicity (including plantar-palmar erythema and gastrointestinal toxicity).

Brief guidance on initial dose modifications at the first appearance of toxicity is given below. Users of these guidelines should also refer to the more detailed guidance contained within the Summary of Product Characteristics (SPC) which can be viewed at [www.medicines.org.uk](http://www.medicines.org.uk).

This includes details on how to manage 2nd and subsequent appearance of toxicities. Toxicity can be managed by symptomatic treatment and/or modification of the dose (treatment interruption or dose reduction). Once the dose has been reduced it should not be increased at a later time. Dose limiting toxicities include diarrhoea, abdominal pain, nausea, stomatitis and handfoot syndrome.
Diarrhoea
If grade 2, 3 or 4 diarrhoea occurs, administration should be immediately interrupted until this resolves or decreases in intensity to Grade 1.
Following Grade 3 diarrhoea doses should be decreased (usual practice is initial 25% dose decrease).
Treatment should be discontinued permanently in the event of Grade 4 diarrhoea.

Handfoot syndrome
If Grade 2 or Grade 3 occurs, administration should be interrupted until the event resolves or decreases in intensity to Grade 1. Following grade 3 handfoot syndrome, subsequent doses of capecitabine should be reduced.

Toxicity Grades Dose changes within a treatment cycle Dose adjustment for next cycle/dose (% of starting dose)

| * Grade 1 | Maintain dose level | Maintain dose level |
| * Grade 2 |                        |                      |
| - 1st appearance | Interrupt until resolved to grade 0-1 | 100% |
| - 2nd appearance | Interrupt until resolved to grade 0-1 | 75% |
| - 3rd appearance | Interrupt until resolved to grade 0-1 | 50% |
| - 4th appearance | Discontinue treatment permanently | Not applicable |
| * Grade 3 |                        |                      |
| - 1st appearance | Interrupt until resolved to grade 0-1 | 75% |
| - 2nd appearance | Interrupt until resolved to grade 0-1 | 50% |
| - 3rd appearance | Discontinue treatment permanently | Not applicable |
| * Grade 4 |                        |                      |
| - 1st appearance | Discontinue permanently OR If physician deems it to be in the patient's best interest to continue, interrupt until resolved to grade 0-1 | 50% |
| - 2nd appearance | Discontinue permanently | Not applicable |

INVESTIGATIONS
Routine Blood test
1) Blood results required before chemotherapy administration

<table>
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<tr>
<th></th>
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<th>Discuss</th>
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Serum creatinine - GFR should be calculated or measured using EDTA
CONCURRENT MEDICATION
Patients taking phenytoin concomitantly with capecitabine should be regularly monitored for increased phenytoin plasma concentrations.

Capecitabine enhances the anticoagulant effects of warfarin. Patients taking warfarin concomitantly with capecitabine must have regular monitoring of INR.

ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (handfoot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Diarrhoea – treat with loperamide or codeine
Cardiotoxicity- special attention is advisable in treating patients with a history of heart disease, arrhythmias or angina pectoris or those who develop chest pain during treatment with capecitabine.
CYCLOPHOSPHAMIDE +/- METHOTREXATE

**Indication:** Metastatic breast cancer, heavily pre-treated patients

**DRUG REGIMEN**
Days 1 to 7  CYCLOPHOSPHAMIDE 50mg PO
Days 1 & 2  METHOTREXATE 2.5mg PO bd

*Cycle Frequency: Every 7 days continuously*

**DOSE MODIFICATIONS**
Previous neutropenic sepsis, discuss with Consultant or Registrar

**Methotrexate**
- GFR 45 - 60mL/min give 65% dose
- GFR 30 - 45mL/min give 50% dose
- GFR < 30mL/min omit dose
- Bilirubin 53 - 85micromol/L or ALT//AST > 180 give 75% dose
- Bilirubin >85 micromol/L omit

**Cyclophosphamide**
- GFR >50ml/min give 100% dose
- GFR 10-50ml/min give 75% dose
- GFR <10ml/min give 50% dose

**INVESTIGATIONS**
Routine Blood test 1) Blood results required before chemotherapy administration

<table>
<thead>
<tr>
<th>Test</th>
<th>Required Ranges</th>
<th>Action</th>
</tr>
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<tbody>
<tr>
<td>Hb x g/dL</td>
<td>≥10, &lt; 10</td>
<td>Give</td>
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<td>≥1.5, &lt; 1.5</td>
<td>Give</td>
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2) Non urgent blood tests

Tests relating to disease response/progression

**CONCURRENT MEDICATION**
None

**ANTIEMETIC POLICY**
Moderately emetogenic

**ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS**
Methotrexate induced mucositis - folic acid (calcium folinate) rescue (see concurrent medication)
Cyclophosphamide may irritate bladder, drink copious volumes of water.
NICE guidance – www.nice.org.uk
In the treatment of locally advanced or metastatic breast cancer, capecitabine in combination with docetaxel is recommended in preference to single agent docetaxel in people for whom anthracycline containing regimens are unsuitable or have failed.

DRUG REGIMEN

Day 1
PREMEDICATION: DEXAMETHASONE 8mg BD starting 24 hours before chemotherapy (or 20mg IV on day of chemotherapy) and 8mg bd post-chemotherapy for 2 days (for patients who are unable to tolerate high doses of steroids 4mg doses may be considered)

DOCETAXEL 75mg/m² in 250ml sodium chloride 0.9% infusion over 1 hour

Days 1 to 14 *CAPECITABINE 1250mg/m² bd po (2500mg/m²/day) days 1 to 14 followed by 7 day rest

NB Capecitabine tablets available as strengths of 150mg and 500mg.

* The Summary of Product Characteristics recommends a dose of 1250mg/m² bd. However 50% of the patients in the main phase 3 trial required a reduction of capecitabine dose. This dose reduction was not associated with any increased risk of progression or resistance to treatment, in fact there was slightly better controlled disease in those whose dose reduced by 25% in the oral Capecitabine arm. Therefore a lower starting dose of 1000*mg/m² bd may be considered.

Cycle Frequency: Every 21 days for 6 cycles subject to tolerance and response

DOSE MODIFICATIONS

Capecitabine
Check CrCl prior to every cycle
CrCl (ml/min) >50 give 100% dose
30 - 50 give 75% dose
<30 contraindicated

Hepatic impairment – SPC recommends interruption of capecitabine therapy if treatment related elevations in bilirubin of > 3 x ULN or ALT/AST > 2.5 x ULN occur.
Treatment may be resumed when bilirubin decreases to < 3 x ULN or hepatic aminotransferases decrease to < 2.5 x ULN.

Please refer to summary of product characteristics for detailed guidance on dose modifications due to toxicity (including plantar palmar erythema and gastrointestinal toxicity).
Toxicity can be managed by symptomatic treatment and/or modification of the dose (treatment interruption or dose reduction). Once the dose has been reduced it should not be increased at a later time. Dose limiting toxicities include diarrhoea, abdominal pain, nausea, stomatitis and handfoot syndrome.

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<td>50%</td>
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<td>- 4th appearance</td>
<td>Discontinue treatment permanently</td>
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<td></td>
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**Docetaxel**

Discuss if severe cutaneous reactions, peripheral neuropathy or fluid retention after previous course.

Hepatic impairment: Patients who have both elevations of transaminases (ALT and/or AST) > 1.5 x ULN and ALP > 2.5 x ULN: recommended SPC dose is 75mg/m². Patients with serum bilirubin > ULN and/or ALT and AST > 3.5 x ULN associated with ALP > 6 x ULN: docetaxel should not be used unless strictly indicated.

Haematology

Treatment should only be readministered when the neutrophil count is > 1.5 x 10⁹/L.

Patients with neutropenia < 0.5 x 10⁹/L for more than one week, or febrile neutropenia, should have the docetaxel dose reduced from 75mg/m² to 55mg/m².

If grade 4 neutropenia or febrile neutropenia occurs at 55mg/m² docetaxel, docetaxel should be discontinued.
INVESTIGATIONS

Routine Blood test
1) Blood results required before chemotherapy administration
   - Give
   - Discuss
   - Hb x g/dL ≥10 < 10
   - Plt x 10^9/L ≥100 < 100
   - Neutrophils x 10^9/L ≥1.5 < 1.5

Serum creatinine - GFR should be calculated or measured using EDTA

2) Non urgent blood tests. Tests relating to disease response/progression

CONCURRENT MEDICATION

Patients taking phenytoin concomitantly with capecitabine should be regularly monitored for increased phenytoin plasma concentrations.

Capecitabine enhances the anticoagulant effects of warfarin.

Patients taking warfarin concomitantly with capecitabine must have regular monitoring of INR.

Docetaxel: Ensure pre-medication is given this can reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions.

ANTIEMETIC POLICY

Low emetic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Palmar plantar (handfoot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds

Diarrhoea – treat with loperamide or codeine
DOCETAXEL 100 with CAPECITABINE 1000

NICE guidance – www.nice.org.uk
In the treatment of locally advanced or metastatic breast cancer, capecitabine in combination with docetaxel is recommended in preference to single agent docetaxel in people for whom anthracycline containing regimens are unsuitable or have failed.

DRUG REGIMEN

Day 1 PREMEDICATION: DEXAMETHASONE 8mg BD starting 24 hours before chemotherapy (or 20mg IV on day of chemotherapy) and 8mg bd post-chemotherapy for 2 days (for patients who are unable to tolerate high doses of steroids 4mg doses may be considered)
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Cycle frequency: Every 7 days for 6 cycles subject to tolerance and response

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Treatment should only be readministered when the neutrophil count is > 1.5 x 10^9/L. Patients with neutropenia < 0.5 x 10^9/L for more than one week, or febrile neutropenia, should have the docetaxel dose reduced by 25%. If grade 4 neutropenia or febrile neutropenia occurs at 55mg/m^2 docetaxel, docetaxel should be discontinued.
INVESTIGATIONS

Routine Blood test
1) Blood results required before chemotherapy administration

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2) Non urgent blood tests. Tests relating to disease response/progression

CONCURRENT MEDICATION
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Patients taking warfarin concomitantly with capecitabine must have regular monitoring of INR.

Docetaxel: Ensure pre-medication is given this can reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions

ANTIEMETIC POLICY
Low emetic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (handfoot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Diarrhoea – treat with loperamide or codeine
DOXORUBICIN 75

Indication: Metastatic breast cancer

DRUG REGIMEN
Day 1 DOXORUBICIN 75mg/m² IV bolus

NB Reduce dose for heavily pretreated patients discuss with consultant (e.g. 60mg/m²)

Cycle Frequency: Every 21 days for 6 cycles

DOSE MODIFICATIONS

Doxorubicin
Dose reduce in severe renal impairment.
Bilirubin 20-50micromol/L give 50% dose
Bilirubin 51-85micromol/L give 25% dose
Bilirubin >85micromol/L omit
If ALT/AST is 2-3 x ULN give 75% dose
If ALT/AST is >3 x ULN give 50% dose
Maximum cumulative dose = 450-550mg/m² (in normal cardiac function)
= 400 mg/m² (in patients with cardiac dysfunction or exposed to mediastinal irradiation)

INVESTIGATIONS
Routine blood test
1) Blood results required before chemotherapy administration
   Give  Discuss
   Hb x g/dL  ≥10   < 10
   Plt x 10⁹/L  ≥100  < 100
   Neutrophils x 10⁹/L  ≥1.5  < 1.5

2) Non urgent blood tests
   • Tests relating to disease response/progression
   • ECG (possible ECHO) required if patient has preexisting cardiac disease (Doxorubicin)

CONCURRENT MEDICATION

ANTIEMETIC POLICY
Moderately emetogenic

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Cardiotoxicity – monitor cardiac function. Doxorubicin may be stopped in future cycles if signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue.
DOXORUBICIN 20 (7 day)

*Indication: Metastatic breast cancer*

**DRUG REGIMEN**
Day 1 **DOXORUBICIN** 20mg/m² IV bolus

NB Dose can be increased in patients who tolerate treatment to the full Doxorubicin (21 day) dose (see separate protocol) discuss with consultant

**Cycle Frequency: Every 7 days (number of cycles to be individualized)**

**DOSE MODIFICATIONS**

*Doxorubicin*
Dose reduce in severe renal impairment.
- Bilirubin 20-50micromol/L give 50% dose
- Bilirubin 51-85micromol/L give 25% dose
- Bilirubin >85micromol/L omit
If ALT/AST is 2-3 x ULN give 75% dose
If ALT/AST is >3 x ULN give 50% dose
Maximum cumulative dose = 450-550mg/m² (in normal cardiac function)
= 400 mg/m² (in patients with cardiac dysfunction or exposed to mediastinal irradiation)

**INVESTIGATIONS**
Routine blood test
1) Blood results required before chemotherapy administration
   - Give
   - Discuss
   - Hb x g/dL ≥10 < 10
   - Plt x 10⁹/L ≥100 < 100
   - Neutrophils x 10⁹/L ≥1.5 < 1.5
2) Non urgent blood tests
   - Tests relating to disease response/progression
   - ECG (possible ECHO) required if patient has preexisting cardiac disease (Doxorubicin)

**CONCURRENT MEDICATION**

**ANTIEMETIC POLICY**
Moderately emetogenic

**ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS**
Cardiotoxicity – monitor cardiac function. Doxorubicin may be stopped in future cycles if signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue.
EPIRUBICIN 60

*Indication: Metastatic breast cancer*

**DRUG REGIMEN**

Day 1 EPIRUBICIN 60mg/m² IV bolus

*Cycle Frequency: Every 21 days for 6 cycles*

**DOSE MODIFICATIONS**

*Epirubicin*

- Bilirubin 20-50 micromol/L give 50% dose
- Bilirubin 51-85 micromol/L give 25% dose
- Bilirubin >85 micromol/L omit

Dose reduce in severe renal impairment.

Maximum lifetime dose = 650mg/m² (in patients with cardiac dysfunction or exposed to mediastinal irradiation)

= 1000mg/m² (with normal cardiac function)

**INVESTIGATIONS**

Routine blood test
1) Blood results required before chemotherapy administration

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2) Non urgent blood tests
- Tests relating to disease response/progression
- ECG (possible ECHO) required if patient has preexisting cardiac disease (Epirubicin)

**CONCURRENT MEDICATION**

**ANTIEMETIC POLICY**

Moderately emetogenic

**ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS**

Cardiotoxicity – monitor cardiac function. Epirubicin may be stopped in future cycles if signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue.
EPIRUBICIN 20 (7 day)

Indication: Metastatic breast cancer

DRUG REGIMEN

Day 1 EPIRUBICIN 20mg/m² IV bolus

Cycle Frequency: Every 7 days (number of cycles to be individualized)

DOSE MODIFICATIONS

Epirubicin
Bilirubin 20-50 micromol/L give 50% dose
Bilirubin 51-85 micromol/L give 25% dose
Bilirubin >85 micromol/L omit
Dose reduce in severe renal impairment.
Maximum lifetime dose = 650mg/m² (in patients with cardiac dysfunction or exposed to mediastinal irradiation)
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INVESTIGATIONS

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2) Non urgent blood tests
   - Tests relating to disease response/progression
   - ECG (possible ECHO) required if patient has preexisting cardiac disease (Epirubicin)

CONCURRENT MEDICATION

ANTIEMETIC POLICY

Moderately emetogenic

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Cardiotoxicity – monitor cardiac function. Epirubicin may be stopped in future cycles if signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue.
ERIBULIN

Indication: Metastatic breast cancer, previously treated with at least 2 previous lines of chemotherapy for advanced disease (including an anthracycline and taxane, unless the patient is unsuitable for these treatments. Performance status 0 to 2.

(Need to apply for funding prior to prescribing)

DRUG REGIMEN
Days 1 and 8
ERIBULIN 1.23mg/m² in 100ml sodium chloride 0.9% IV infusion over 5 minutes
Eribulin equivalent to eribulin mesylate 1.4mg/m²)

Cycle Frequency: Every 21 days

DOSE MODIFICATIONS
Eribulin
In severe renal impairment (Creatinine clearance <40ml/min) may need a dose reduction.

Hepatic impairment
Mild hepatic impairment (Child-Pugh A) give 0.97mg/m².
Moderate hepatic impairment (Child-Pugh B) give 0.62mg/m².
Severe hepatic impairment (Child-Pugh C) has not been studied but it is expected that a more marked dose reduction is needed if eribulin is used in these patients.

The score employs five clinical measures of liver disease. Each measure is scored 1-3, with 3 indicating the most severe derangement.

<table>
<thead>
<tr>
<th>Measure</th>
<th>1 point</th>
<th>2 points</th>
<th>3 points</th>
</tr>
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<tbody>
<tr>
<td>Total bilirubin μmol/l</td>
<td>&lt;34</td>
<td>34-50</td>
<td>&gt;50</td>
</tr>
<tr>
<td>Serum albumin g/l</td>
<td>&gt;35</td>
<td>28-35</td>
<td>&lt;28</td>
</tr>
<tr>
<td>INR</td>
<td>&lt;1.7</td>
<td>1.7-2.20</td>
<td>&gt;2.20</td>
</tr>
<tr>
<td>Ascites</td>
<td>None</td>
<td>Mild</td>
<td>Severe</td>
</tr>
<tr>
<td>Hepatic encephalopathy</td>
<td>None</td>
<td>Grade I-II</td>
<td>Grade III-IV (or refractory)</td>
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(or suppressed with medication)
Adverse reaction after previous Eribulin administration

**Recommended dose**

**Haematological:**
- ANC < 0.5 x 10^9/l lasting more than 7 days
- ANC < 1 x 10^9/l neutropenia complicated by fever or infection
- Platelets < 25 x 10^9/l thrombocytopenia
- Platelets < 50 x 10^9/l thrombocytopenia complicated by haemorrhage or requiring blood or platelet transfusion

**Non-haematological:**
- Any Grade 3 or 4 in the previous cycle

- Reoccurrence of any haematological or non-haematological adverse reactions as specified above
  - Despite reduction to 0.97 mg/m²
  - Despite reduction to 0.62 mg/m²

- Consider discontinuation

Do not re-escalate the eribulin dose after it has been reduced.

**INVESTIGATIONS**

Routine Blood test
1) Blood results required before chemotherapy administration

- **Give**
  - Hb x g/dL ≥10 < 10
  - Plt x 10^9/L ≥100 < 100
  - Neutrophils x 10^9/L ≥1.5 < 1.5

- **Discuss**

ECG (possibly ECHO) required if patient has pre-existing cardiac disease

**CONCURRENT MEDICATION**
None

**ANTIEMETIC POLICY**
Moderate emetogenic risk

**ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS**
Myelosuppression
Peripheral neuropathy
QT prolongation

**REFERENCES**
1. SPC March 2011
LAPATINIB and CAPECITABINE

**Indication:** Advanced breast cancer
(Need to apply for funding prior to prescribing)

**DRUG REGIMEN**
Day 1 LAPATINIB 1250mg po once daily continuously
Days 1 to 14 CAPECITABINE 1000mg/m^2 twice daily (2000mg/m^2/day) po followed by a 7 day rest

NB Capecitabine tablets available as strengths of 150mg and 500mg.
Lapatinib tablets available as strengths of 250mg

**Cycle Frequency:** Every 21 days

**DOSE MODIFICATIONS**

**Lapatinib**
Caution is advised in patients with severe renal impairment as there is no experience of lapatinib in this population. No dose adjustment is necessary in patients with mild to moderate renal impairment.
Lapatinib should be discontinued if changes in liver function are severe and patients should not be retreated.
Administration of lapatinib to patients with moderate to severe hepatic impairment should be undertaken with caution due to increased exposure to the medicinal product. Insufficient data are available in patients with hepatic impairment to provide a dose adjustment recommendation.

**Capecitabine**
Check CrCl prior to every cycle
CrCl (ml/min) >50 give 100% dose
30 - 50 give 75% dose
<30 contraindicated

Hepatic impairment – SPC recommends interruption of capecitabine therapy if treatment related elevations in bilirubin of > 3 x ULN or ALT/AST > 2.5 x ULN occur.
Treatment may be resumed when bilirubin decreases to < 3 x ULN or hepatic aminotransferases decrease to < 2.5 x ULN.
Please refer to summary of product characteristics for detailed guidance on dose modifications due to toxicity (including plantar palmar erythema and gastrointestinal toxicity).

Toxicity can be managed by symptomatic treatment and/or modification of the dose (treatment interruption or dose reduction). Once the dose has been reduced it should not be increased at a later time. Dose limiting toxicities include diarrhoea, abdominal pain, nausea, stomatitis and handfoot syndrome.
<table>
<thead>
<tr>
<th>Toxicity Grades</th>
<th>Dose changes within a treatment cycle</th>
<th>Dose adjustment for next cycle/dose (% of starting dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Grade 1</td>
<td>Maintain dose level</td>
<td>Maintain dose level</td>
</tr>
<tr>
<td>* Grade 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- 1st appearance</td>
<td>Interrupt until resolved to grade 0-1</td>
<td>100%</td>
</tr>
<tr>
<td>- 2nd appearance</td>
<td>Interrupt until resolved to grade 0-1</td>
<td>75%</td>
</tr>
<tr>
<td>- 3rd appearance</td>
<td>Interrupt until resolved to grade 0-1</td>
<td>50%</td>
</tr>
<tr>
<td>- 4th appearance</td>
<td>Discontinue treatment permanently</td>
<td>Not applicable</td>
</tr>
<tr>
<td>* Grade 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- 1st appearance</td>
<td>Interrupt until resolved to grade 0-1</td>
<td>75%</td>
</tr>
<tr>
<td>- 2nd appearance</td>
<td>Interrupt until resolved to grade 0-1</td>
<td>50%</td>
</tr>
<tr>
<td>- 3rd appearance</td>
<td>Discontinue treatment permanently</td>
<td>Not applicable</td>
</tr>
<tr>
<td>* Grade 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- 1st appearance</td>
<td>Discontinue permanently OR</td>
<td></td>
</tr>
<tr>
<td></td>
<td>If physician deems it to be in the</td>
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<tr>
<td></td>
<td>patient's best interest to continue,</td>
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<tr>
<td></td>
<td>interrupt until resolved to grade 0-1</td>
<td></td>
</tr>
<tr>
<td>- 2nd appearance</td>
<td>Discontinue permanently</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

**INVESTIGATIONS**

Routine Blood test

1) Blood results required before chemotherapy administration

<table>
<thead>
<tr>
<th>Give</th>
<th>Discuss</th>
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</thead>
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<td>≥100</td>
</tr>
<tr>
<td>Neutrophils x 10^9/L</td>
<td>≥1.5</td>
</tr>
</tbody>
</table>

Serum creatinine - GFR should be calculated or measured using EDTA

**CONCURRENT MEDICATION**

Patients taking phenytoin concomitantly with capecitabine should be regularly monitored for increased phenytoin plasma concentrations.

Capecitabine enhances the anticoagulant effects of warfarin.

Patients taking warfarin concomitantly with capecitabine must have regular monitoring of INR.

**ANTIEMETIC POLICY**

Low emetogenic risk
ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Palmar plantar (hand foot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds
Diarrhoea – treat with loperamide or codeine
Cardiac – lapatinib should be discontinued in patients with symptoms associated with decreased left ventricular ejection fraction (LVEF) that are NCI CTCAE grade 3 or greater or if their LVEF drops below the institutions lower limit of normal. Lapatinib may be restarted at a reduced dose (1000mg/day) after a minimum of 2 weeks and if the LVEF recovers to normal and the patient is asymptomatic.
Pulmonary – Lapatinib should be discontinued in patients who experience pulmonary symptoms which are NCI CTCAE grade 3 or greater.

REFERENCES
1. SPC Lapatinib
2. SPC Capecitabine
Indication: Metastatic breast cancer

DRUG REGIMEN
Day 1  MITOMYCIN 10mg IV bolus (alternate cycles)
       MITOXANTRONE 10mg in 50ml sodium chloride 0.9% infusion over 15 minutes
       METHOTREXATE 50mg IV bolus

Cycle Frequency: Every 21 days for 6 cycles

DOSE MODIFICATIONS
Mitoxantrone
Bilirubin >60 micromol/L and good performance status give 60% dose
Bilirubin >60 micromol/L and poor performance status omit
Maximum cumulative dose = 110mg/m²

Methotrexate
GFR 45 - 60mL/min give 65% dose
GFR 30 - 45mL/min give 50% dose
GFR < 30mL/min omit dose
Bilirubin 53 - 85 micromol/L or ALT/AST > 180 give 75% dose
Bilirubin >85 micromol/L omit

Mitomycin
GFR > 10ml/min give 100% dose
GFR < 10ml/min give 75% dose
Consider a dose reduction for high doses of Mitomycin when GFR 10-60ml/min

INVESTIGATIONS
Routine Blood test 1) Blood results required before chemotherapy administration

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<td>≥1.5</td>
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</table>

2) Non urgent blood tests
Tests relating to disease response/progression
CONCURRENT MEDICATION
Calcium folinate (calcium leucovorin) 15mg PO/IV every 6 hours for 6 doses starting 24 hours after Methotrexate if:
  . Pleural effusions/ascites
  . Previous mucositis
  . Serum creatinine > 120 micromols/L

ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Cardiotoxicity – monitor cardiac function. Mitoxantrone may be stopped in future cycles if signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue.
Methotrexate induced mucositis - folinic acid (calcium folinate) rescue (see concurrent medication)
DOCETAXEL 100 metastatic (21 day)

**Indication: Anthracycline resistant breast cancer, metastatic breast cancer**

**NICE guidance – www.nice.org.uk**
Docetaxel and paclitaxel are recommended as an option for the treatment of advanced breast cancer where initial cytotoxic chemotherapy (including an anthracycline) has failed or is inappropriate.

**DRUG REGIMEN**

**Day 1**   
**PREMEDICATION:** DEXAMETHASONE 8mg BD starting 24 hours before chemotherapy (or 20mg IV on day of chemotherapy) and 8mg bd post-chemotherapy for 2 days (for patients who are unable to tolerate high doses of steroids 4mg doses may be considered)

DOCETAXEL 100mg/m² in 250ml sodium chloride 0.9% infusion over 1 hour

NB Reduce docetaxel to 75mg/m² in heavily pretreated patients or performance status not optimal

**Cycle Frequency: Every 21 days usually no more than 6 (subject to tolerance and response)**

**DOSE MODIFICATIONS**
Discuss if severe cutaneous reactions, peripheral neuropathy or fluid retention after previous course.

Hepatic impairment: Patients who have both elevations of transaminases (ALT and/or AST) > 1.5 x ULN and ALP > 2.5 x ULN: recommended SPC dose is 75mg/m2.
Patients with serum bilirubin > ULN and/or ALT and AST > 3.5 x ULN associated with ALP > 6 x ULN: docetaxel should not be used unless strictly indicated.

**INVESTIGATIONS**

Routine Blood test
1) Blood results required before chemotherapy administration

<table>
<thead>
<tr>
<th>Test</th>
<th>Lower Limit</th>
<th>Upper Limit</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL</td>
<td>≥10</td>
<td>&lt; 10</td>
<td>Discuss</td>
</tr>
<tr>
<td>Plt x 10⁹/L</td>
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<td>&lt; 1.5</td>
<td></td>
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</tbody>
</table>

2) Non urgent blood tests.
Tests relating to disease response/progression
CONCURRENT MEDICATION
Ensure premedication given. This can reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions.

ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Discuss if severe cutaneous reactions, peripheral neuropathy or fluid retention after previous course
DOCETAXEL 40 (7 day)

**Indication:** Anthracycline resistant breast cancer for patients who cannot tolerate the standard three weekly regimen

**DRUG REGIMEN**

Day 1  Premedication  DEXAMETHASONE 8mg BD starting 12 hours before chemotherapy and continued for a total of 3 doses (for patients who are unable to tolerate high doses of steroids or tolerate docetaxel well 4mg bd may be considered).

**DOCETAXEL** 40mg/m² in 250ml sodium chloride 0.9% infusion over 1 hour

Day 8  Premedication  DEXAMETHASONE 8mg BD starting 12 hours before chemotherapy and continued for a total of 3 doses (for patients who are unable to tolerate high doses of steroids or tolerate docetaxel well 4mg bd may be considered).

**DOCETAXEL** 40mg/m² in 250ml sodium chloride infusion over 1 hour

Day 15  Premedication  DEXAMETHASONE 8mg BD starting 12 hours before chemotherapy and continued for a total of 3 doses (for patients who are unable to tolerate high doses of steroids or tolerate docetaxel well 4mg bd may be considered).

**DOCETAXEL** 40mg/m² in 250ml sodium chloride 0.9% infusion over 1 hour

**Cycle Frequency:** Every 28 days for 6 cycles

**DOSE MODIFICATIONS**

Discuss if severe cutaneous reactions, peripheral neuropathy or fluid retention after previous course.

Hepatic impairment: Patients who have both elevations of transaminases (ALT and/or AST) > 1.5 x ULN and ALP > 2.5 x ULN: recommended SPC dose is 75mg/m². Patients with serum bilirubin > ULN and/or ALT and AST > 3.5 x ULN associated with ALP > 6 x ULN: docetaxel should not be used unless strictly indicated.

**INVESTIGATIONS**

Routine Blood test

1) Blood results required before chemotherapy administration

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</tbody>
</table>

2) Non urgent blood tests

Tests relating to disease response/progression
CONCURRENT MEDICATION
Ensure pre-medication is given this can reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions

ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Discuss if severe cutaneous reactions, peripheral neuropathy or fluid retention after previous course
GEMCITABINE and CARBOPLATIN

Indication: Triple negative or BRCA mutated breast cancer

DRUG REGIMEN

Day 1  
GEMCITABINE 1000mg/m² infusion in 250ml sodium chloride 0.9% over 30 minutes  
CARBOPLATIN AUC 4 in 250ml glucose 5% infusion over 60 minutes

Day 8  
GEMCITABINE 1000mg/m² infusion in 250ml sodium chloride 0.9% over 30 minutes

NB In heavily pretreated or elderly patients consider reducing gemcitabine doses to 750mg/m².

Cycle Frequency: Every 21 days for 6 cycles

DOSE MODIFICATIONS

Previous neutropenic sepsis, discuss with Consultant or Registrar

Carboplatin
If GFR = or < 20ml/min discuss with consultant.

Gemcitabine
CrCl <30ml/min consider dose reduction (Clinical decision)

Neutrophils >1.5x10⁹/L and platelets >100x10⁹/L give 100% dose  
Neutrophils<1.5x10⁹/L or platelets <100x10⁹/L delay treatment (Day 1) or omit treatment (Day 8)

Diarrhoea and/or mucositis
Grade 2 toxicity – omit until toxicity resolved then restart at 100% dose  
Grade 3 toxicity – omit until toxicity resolved then restart 25% dose reduction  
Grade 4 toxicity – omit until toxicity resolved then restart 50% dose reduction
INVESTIGATIONS
Pre assessment requiremets
FBC and biochem – for CrCl pre cycle 1 (biochem and FBC to be done each time)

Routine Blood test 1) Blood results required before chemotherapy administration

Give Discuss

Hb x g/dL ≥10 < 10
Platelets x 10^9/L ≥100 < 100
Neutrophils x 10^9/L ≥1.5 < 1.5

Liver function tests (LFT)

- GFR assessed using 51Cr-EDTA result or calculated creatinine clearance at the Consultant’s discretion.
- Patients with hydronephrosis or serum creatinine ≥ 100 micromol/L need a serum creatinine checked every cycle. All patients have serum creatinine checked 1st and 4th cycle.

2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION
Anaphylaxis treatment should be prescribed if the patient has had an anaphylactic episode previously.

DEXAMETHASONE 20mg IV bolus
CHLORPHENAMINE 10mg IV bolus
RANITIDINE 50mg IV bolus
Carboplatin should be given at a slower rate e.g. 2-4 hours.

ANTIEMETIC POLICY
Moderate emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Ototoxicity - monitor
Neurotoxicity - monitor
Diarrhoea – see dose modifications
Mucositis – see dose modifications
PACLITAXEL 175 (21 day)

NICE guidance – www.nice.org.uk
Docetaxel and paclitaxel are recommended as an option for the treatment of advanced breast cancer where initial cytotoxic chemotherapy (including an anthracycline) has failed or is inappropriate

DRUG REGIMEN
Day 1  PREMEDICATION 30mins prior to infusion:
DEXAMETHASONE 20 mg IV bolus
RANITIDINE 50 mg IV bolus
CHLORPHENAMINE 10 mg IV bolus
PACLITAXEL 175mg/m² in 500ml sodium chloride 0.9% infusion over 3 hours

Cycle Frequency: Every 21 days up to 6 cycles subject to tolerance and response

DOSE MODIFICATIONS
Previous neutropenic sepsis, discuss with Consultant or Registrar
If patient complains of tinnitus, tingling of fingers and/or toes or motor weakness discuss with Consultant or Registrar before administration
If grade >= 2 neuropathy, consider using paclitaxel 135 mg/m²
In the absence of Gilbert's syndrome:
Bilirubin <1.25xULN and ALT/AST <10xULN dose at 175mg/m²
Bilirubin <27 micromol/L give 135mg/m²
Bilirubin 27-51micromol/L give 75mg/m²
Bilirubin >51micromol/L give 50mg/m²

Dose escalation possible. 200mg/m² on second and subsequent cycles if nadir count is satisfactory. Discuss with Consultant or Registrar

INVESTIGATIONS
Routine Blood test 1) Blood results required before chemotherapy administration

Give  Discuss
Hb x g/dL   ≥10 < 10
Plt x 10⁹/L ≥100 < 100
Neutrophils x 10⁹/L ≥1.5 < 1.5

Liver function tests (LFT)

2) Non urgent blood tests
Tests relating to disease response/progression
CONCURRENT MEDICATION
Ensure pre medication given

ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
(2% risk of severe hypersensitivity)
Reactions range from mild hypotension (light-headedness) to full cardiac collapse (anaphylactic shock). Discontinue infusion and resuscitate appropriate to reaction. If reaction is mild and settles promptly (i.e. within 5-10 minutes), cautiously restart at a slower rate under close supervision. If further reactions occur stop treatment.
PACLITAXEL 90mg (7 day)

Indication: Metastatic or locally advanced breast cancer (weekly schedule is not licensed treatment).

DRUG REGIMEN

Day 1  PREMEDICATION 30mins prior to infusion:
- DEXAMETHASONE 8mg IV bolus
- RANITIDINE 50mg IV bolus
- CHLORPHENAMINE 10mg IV bolus

PACLITAXEL 90mg/m² in 500ml sodium chloride 0.9% infusion over 1 hour

Cycle Frequency: Every 7 days for 12 weeks (3 x 28 days)

NB Patients who are elderly, had extensive bone irradiation or bone secondaries or having this as 3rd line treatment may require a reduced dose day 1, 8 and 15 every 28 days (see separate protocol)

DOSE MODIFICATIONS

If patient complains of tinnitus, tingling of fingers and/or toes or motor weakness discuss with Consultant or Registrar before administration.

In the absence of Gilbert’s syndrome:
Bilirubin >51micromol/L stop treatment

INVESTIGATIONS

Routine Blood test
1) Blood results required before chemotherapy administration

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<td>&lt; 1.5</td>
</tr>
</tbody>
</table>

Liver function tests (LFT)

2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION

Ensure pre-medication is given.
ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
(2% risk of severe hypersensitivity)
Reactions range from mild hypotension (light-headedness) to full cardiac collapse (anaphylactic shock). Discontinue infusion and resuscitate appropriate to reaction. If reaction is mild and settles promptly (i.e. within 5-10 minutes), cautiously restart at a slower rate under close supervision. If further reactions occur stop treatment.
PACLITAXEL 80mg (7 day)

Indication: Metastatic or locally advanced breast cancer (weekly schedule is not licensed treatment). For patients who require a reduced dose e.g. elderly, had extensive bone irradiation or bone secondaries or having this as 3rd line treatment

DRUG REGIMEN
Day 1  PREMEDICATION 30mins prior to infusion:
DEXAMETHASONE 8mg IV bolus
RANITIDINE 50mg IV bolus
CHLORPHENAMINE 10mg IV bolus

PACLITAXEL 80mg/m² in 500ml sodium chloride 0.9% infusion over 1 hour

Cycle Frequency: Days 1, 8 and 15 every 28 days up to 3 cycles subject to tolerance and response

DOSE MODIFICATIONS
If patient complains of tinnitus, tingling of fingers and/or toes or motor weakness discuss with Consultant or Registrar before administration.

In the absence of Gilbert's syndrome:
Bilirubin >51micromol/L stop treatment

INVESTIGATIONS
Routine Blood test
1) Blood results required before chemotherapy administration

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Liver function tests (LFT)

2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION
Ensure pre-medication is given.
ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
(2% risk of severe hypersensitivity)
Reactions range from mild hypotension (light-headedness) to full cardiac collapse (anaphylactic shock). Discontinue infusion and resuscitate appropriate to reaction. If reaction is mild and settles promptly (i.e. within 5-10 minutes), cautiously restart at a slower rate under close supervision. If further reactions occur stop treatment.

Paclitaxel
80mg weekly q28d

Breast TSSG Chair Authorisation:
Date:

Page 2 of 2 Published: March 2012
Review: March 2014
Version 3.2

Network Chemotherapy Protocols – Breast Cancer 66
PACLITAXEL albumin bound

Indication: Metastatic breast cancer, only patients who have received previous treatment and who cannot tolerate either docetaxel or solvent bound paclitaxel.

DRUG REGIMEN
Day 1  PACLITAXEL ALBUMIN BOUND  260mg/m² IV infusion over 30 minutes

Cycle Frequency: Every 21 days up to 6 cycles subject to tolerance and response

DOSE MODIFICATIONS
If patient complains of tinnitus, tingling of fingers and/or toes or motor weakness discuss with Consultant or Registrar before administration.
Hepatic - Mild to moderate hepatic impairment there is insufficient data. Patients with severe hepatic impairment should not be treated with paclitaxel.
Renal - Insufficient data to recommend dose modifications in patients with renal impairment.

INVESTIGATIONS
Routine Blood test
1) Blood results required before chemotherapy administration

Give  Discuss
Hb x g/dL  ≥10  < 10
Plt x 10^9/L  ≥100  < 100
Neutrophils x 10^9/L  ≥1.5  < 1.5
Liver function tests (LFT)

2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION
None

ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Hypersensitivity - discontinue immediately
Sensory neuropathy
Cardiotoxicity

REFERENCES
1. SPC July 2011
2. MOBBB recommendation July 2011
**PACLITAXEL CARBOPLATIN 21 day**

*Indication: Triple negative recurrent / metastatic breast cancer*

**DRUG REGIMEN**

*Day 1* PRE-MEDICATION 30mins prior to paclitaxel
- **DEXAMETHASONE** 20mg IV bolus
- **RANITIDINE** 50mg IV bolus
- **CHLORPHENAMINE** 10mg IV bolus
- **PACLITAXEL** 175mg/m² in 500ml sodium chloride 0.9% infusion over 3 hours (PVC free)
- **CARBOPLATIN** AUC 6 (EDTA) in 500ml Glucose 5% infusion over 60 minutes

Dose (mg) = (GFR + 25) x AUC

*Cycle Frequency: Every 21 days for 6 cycles (may be given for 8 cycles in certain circumstances)*

**DOSE MODIFICATIONS**

Previous neutropenic sepsis, discuss with Consultant or Registrar

**Carboplatin**
If GFR/CrCl = or <20ml/min discuss with consultant.

**Paclitaxel**
If patient complains of tinnitus, tingling of fingers and/or toes or motor weakness discuss with Consultant or Registrar before administration. If grade II or > neuropathy, consider using paclitaxel 135mg/m².

- Bilirubin <1.25xULN and AST <10xULN dose at 175mg/m²
- Bilirubin <26micromol/L give 135mg/m²
- Bilirubin 27-51micromol/L give 75mg/m²
- Bilirubin >51micromol/L give 50mg/m²

**INVESTIGATIONS**

Routine Blood test 1) Blood results required before chemotherapy administration

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</tbody>
</table>
a. Liver function tests (LFTs)
b. GFR assessed using $^{51}$Cr-EDTA result or calculated creatinine clearance at the Consultant’s discretion. (Carboplatin)
c. Patients with hydronephrosis or serum creatinine $\geq$ 100micromol/L need a serum creatinine checked every cycle. All patients have serum creatinine checked 1st and 4th cycle - Carboplatin.

2) Non-urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION
Paclitaxel – ensure pre medication is given
Carboplatin - Anaphylaxis treatment should be prescribed if the patient has had an anaphylactic episode previously. Carboplatin should be given at a slower rate e.g. 2-4 hours.

ANTIEMETIC POLICY
Moderately emetogenic (routinely dexamethasone and metoclopramide is adequate but 5HT$_3$ antagonist may be required if there is inadequate control).

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
2% risk of severe hypersensitivity. Reactions to paclitaxel range from mild hypotension (light-headedness) to full cardiac collapse (anaphylactic shock). Discontinue infusion and resuscitate appropriate to reaction. If reaction is mild and settles promptly (i.e. within 5-10mins), cautiously restart at a slower rate under close supervision. If further reactions occur stop treatment.
Ototoxicity - monitor
Neurotoxicity – monitor
PACLITAXEL and GEMCITABINE (21 day)

NICE guidance - www.nice.org.uk
Gemcitabine in combination with paclitaxel, within its licensed indication, is recommended as an option for the treatment of metastatic breast cancer only when docetaxel monotherapy or docetaxel plus capecitabine are also considered appropriate.

DRUG REGIMEN
Day 1  PREMEDICATION 30mins prior to infusion:
DEXAMETHASONE 20 mg IV bolus
RANITIDINE 50 mg IV bolus
CHLORPHENAMINE 10 mg IV bolus
PACLITAXEL 175mg/m² in 500ml sodium chloride 0.9% infusion over 3 hours
GEMCITABINE 1250mg/m² infusion in 250ml sodium chloride 0.9% over 30 minutes

Day 8  GEMCITABINE 1250mg/m² infusion in 250ml sodium chloride 0.9% over 30 minutes

Cycle Frequency: Every 21 days for 6 cycles

DOSE MODIFICATIONS
Previous neutropenic sepsis, discuss with Consultant or Registrar

Paclitaxel
If patient complains of tinnitus, tingling of fingers and/or toes or motor weakness discuss with Consultant or Registrar before administration

In the absence of Gilbert's syndrome:
Bilirubin <1.25xULN and AST <10xULN dose at 175mg/m²
Bilirubin <26micromol/L give 135mg/m²
Bilirubin 27-51micromol/L give 75mg/m²
Bilirubin >51micromol/L give 50mg/m²
Gemcitabine
CrCl <30ml/min consider dose reduction (Clinical decision)

Diarrhoea and/or mucositis
Grade 2 toxicity – omit until toxicity resolved then restart at 100% dose
Grade 3 toxicity – omit until toxicity resolved then restart 25% dose reduction
Grade 4 toxicity – omit until toxicity resolved then restart 50% dose reduction

INVESTIGATIONS
Routine Blood test 1) Blood results required before chemotherapy administration

Give
Hb x g/dL ≥10 < 10
Plt x 10^9/L ≥100 < 100
Neutrophils x 10^9/L ≥1.5 < 1.5

Liver function tests (LFT)

2) Non urgent blood tests
Tests relating to disease response/progression

CONCURRENT MEDICATION
Ensure pre medication given -paclitaxel

ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
(2% risk of severe hypersensitivity)
Reactions range from mild hypotension (light-headedness) to full cardiac collapse (anaphylactic shock). Discontinue infusion and resuscitate appropriate to reaction. If reaction is mild and settles promptly (i.e. within 5-10 minutes), cautiously restart at a slower rate under close supervision. If further reactions occur stop treatment.
Diarrhoea – see dose modifications
Mucositis – see dose modifications
TRASTUZUMAB 4/2 (7 day)

**Indication:** Metastatic breast (HER3+ or FISH+)

NICE guidance - www.nice.org.uk

Trastuzumab is used in combination with paclitaxel for people with tumours with excessive human epidermal growth factor receptor 2 (HER2) at levels of 3+ who have not had chemotherapy for metastatic breast cancer and for whom anthracycline treatment is inappropriate.

Trastuzumab monotherapy is recommended for women with tumours with excessive HER2 at levels of 3+ who have had at least two chemotherapy treatments for metastatic breast cancer. Previous chemotherapy must have included at least an anthracycline drug and a taxane drug where these treatments are appropriate. It should also have included hormonal therapy in patients sensitive to oestrogen.

**DRUG REGIMEN**

**Cycle 1 only**

**Day 1 Loading dose** (to be given once only)

*TRASTUZUMAB* 4mg/kg in 250ml sodium chloride 0.9% infusion over 90 minutes

Cycles 2 to 24

**Day 1 Maintenance dose**

TRASTUZUMAB 2mg/kg in 250ml sodium chloride 0.9% infusion over 30** or 90 minutes

*NB.* Patients need to remain on the ward / day unit for monitoring for 6 hours post first dose

**Cycle Frequency:** Every 7 days up to 24 cycles in the first instance subject to tolerance and response

**DOSE MODIFICATIONS**

No dose reduction or cessation of Trastuzumab is required if patient has acute reversible neutropenia

If trastuzumab infusion is delayed by more than 7 days the patient should be reloaded at 4mg/kg.

Continuation and discontinuation of trastuzumab based on interval LVEF assessment

- If LVEF <44 hold trastuzumab, repeat LVEF in 3 weeks.
  - If repeat LVEF <44 or LVEF 45-49 and >10 points from baseline then stop trastuzumab.
  - If repeat LVEF 45-49 and <10 points from baseline or LVEF >49 resume trastuzumab.
- If LVEF 45-49 and >10 EF points from baseline hold trastuzumab, repeat LVEF in 3 weeks.
  - If repeat LVEF <44 or LVEF 45-49 and >10 points from baseline stop trastuzumab.
  - If repeat LVEF 45-49 and <10 points from baseline or LVEF >49 resume trastuzumab.
- If LVEF > 50 or LVEF 45-49 and <10 EF points from baseline continue trastuzumab.

New LVEF assessment results should be available by the day of the next scheduled trastuzumab administration and a decision to give or hold the dose must be made based on this algorithm.
INVESTIGATIONS
Routine Blood test
1) Blood results required before chemotherapy administration

<table>
<thead>
<tr>
<th>Test</th>
<th>Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL</td>
<td>≥10 &lt; 10</td>
</tr>
<tr>
<td>Plt x 10^9/L</td>
<td>≥100 &lt; 100</td>
</tr>
<tr>
<td>Neutrophils x 10^9/L</td>
<td>≥1.5 &lt; 1.5</td>
</tr>
</tbody>
</table>

2) Non urgent blood tests
- Tests relating to disease response/progression
- Baseline weight and every 3 months
- Monitor cardiac function (ECG/ECHO) of all patients before and during treatment, aiming for assessments every 3 months

CONCURRENT MEDICATION
Trastuzumab infusion related chills and/or fevers – treat with paracetamol and chlorphenamine.

ANTIEMETIC POLICY
Low emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Cardiotoxicity – monitor cardiac function.
Trastuzumab infusion related chills and/or fevers are commonly observed during the first infusion (but infrequently with subsequent infusions). Other symptoms may include nausea, hypertension, vomiting, pain, rigors, headache, cough, dizziness, rash, and asthenia.
Some adverse reactions to trastuzumab infusion including dyspnoea, hypotension, wheezing, bronchospasm, supraventricular tachyarrhythmia, reduced oxygen saturation and respiratory distress can be serious and potentially fatal.
If symptoms of back ache, nausea or vomiting, do a set of obs. Give hydrocortisone 100mg IV, chlorphenamine 10mg IV.

NB Patients need to remain on the ward/day unit for monitoring for 6 hours post first dose and for 2 hours post maintenance doses.
Indication: Metastatic breast (HER3+ or FISH +) if weekly administration is inconvenient or impractical

NICE guidance - www.nice.org.uk
Trastuzumab is used in combination with paclitaxel for people with tumours with excessive human epidermal growth factor receptor 2 (HER2) at levels of 3+ who have not had chemotherapy for metastatic breast cancer and for whom anthracycline treatment is inappropriate. Trastuzumab monotherapy is recommended for women with tumours with excessive HER2 at levels of 3+ who have had at least two chemotherapy treatments for metastatic breast cancer. Previous chemotherapy must have included at least an anthracycline drug and a taxane drug where these treatments are appropriate. It should also have included hormonal therapy in patients sensitive to oestrogen.

DRUG REGIMEN
Cycle 1
Day 1 Loading dose (to be given once only)
*TRASTUZUMAB 8mg/kg in 250ml sodium chloride 0.9% infusion over 90 minutes

Cycle 2 to 18
Day 1 Maintenance dose
*TRASTUZUMAB 6mg/kg in 250ml sodium chloride 0.9% infusion over 30** or 90 minutes

*NB. Patients need to remain on the ward / day unit for monitoring for 6 hours post first dose
** If loading dose is tolerated subsequent cycles may be given over 30 minutes.

Cycle Frequency: Every 21 days up to 18 cycles in the first instance to tolerance and response.

DOSE MODIFICATIONS
No dose reduction or cessation of Trastuzumab is required if patient have acute reversible neutropenia
If trastuzumab infusion is delayed by more than 7 days the patient should be reloaded at 8mg/kg.

Continuation and discontinuation of trastuzumab based on interval LVEF assessment
• If LVEF <44 hold trastuzumab, repeat LVEF in 3 weeks.
  If repeat LVEF <44 or LVEF 45-49 and >10 points from baseline then stop trastuzumab.
  If repeat LVEF 45-49 and <10 points from baseline or LVEF >49 resume trastuzumab.
• If LVEF 45-49 and >10 EF points from baseline hold trastuzumab, repeat LVEF in 3 weeks.
  If repeat LVEF <44 or LVEF 45-49 and >10 points from baseline stop trastuzumab.
  If repeat LVEF 45-49 and <10 points from baseline or LVEF >49 resume trastuzumab.
• If LVEF > 50 or LVEF 45-49 and <10 EF points from baseline continue trastuzumab.

New LVEF assessment results should be available by the day of the next scheduled trastuzumab administration and a decision to give or hold the dose must be made based on this algorithm.
INVESTIGATIONS
Routine Blood test
1) Blood results required before chemotherapy administration

   Give    Discuss
   Hb x g/dL    ≥10   < 10
   Plt x 10^9/L    ≥100   < 100
   Neutrophils x 10^9/L    ≥1.5   < 1.5

2) Non urgent blood tests
   • Tests relating to disease response/progression
   • Baseline weight and every 3 months
   • Monitor cardiac function (ECG/ECHO) of all patients before and during treatment, aiming for assessments every 3 months

CONCURRENT MEDICATION
Trastuzumab infusion related chills and/or fevers – treat with paracetamol and chlorphenamine.

ANTIEMETIC POLICY
Minimal emetogenic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
Cardiotoxicity – monitor cardiac function.
Trastuzumab infusion related chills and/or fevers are commonly observed during the first infusion (but infrequently with subsequent infusions). Other symptoms may include nausea, hypertension, vomiting, pain, rigors, headache, cough, dizziness, rash, and asthenia.
Some adverse reactions to trastuzumab infusion including dyspnoea, hypotension, wheezing, bronchospasm, supraventricular tachyarrhythmia, reduced oxygen saturation and respiratory distress can be serious and potentially fatal.
If symptoms of back ache, nausea or vomiting, do a set of obs. Give hydrocortisone 100mg IV, chlorphenamine 10mg IV.
VINORELBINE 30 (21 day)

NICE guidance – www.nice.org.uk
Vinorelbine monotherapy is not recommended as a first line treatment for advanced breast cancer. Vinorelbine monotherapy is recommended as one option for second line or later therapy for the treatment of advanced breast cancer when anthracycline based regimens have failed or are unsuitable.

DRUG REGIMEN
Day 1 VINORELBINE 30mg/m² (maximum 60mg) IV infusion in 50ml sodium chloride 0.9% over 10 minutes
Day 8 VINORELBINE 30mg/m² (maximum 60mg) IV infusion in 50ml sodium chloride 0.9% over 10 minutes
Administration should always be followed by a sodium chloride 0.9% infusion to flush the vein.
NB For heavily pretreated patients or patients with poor performance status, consider giving in a four weekly cycle or reduce dose to 25mg/m² discuss with consultant

Cycle Frequency: Every 21 days for 6 cycles subject to tolerance and response

DOSE MODIFICATIONS
Previous neutropenic sepsis, discuss with Consultant or Registrar
If patients have a neutrophil count <1.5 on day 8, this dose can be delayed to day 15.
AST/ALT ≤5xULN and bilirubin <1.55xULN give 100% dose
AST/ALT 5.1-20xULN and bilirubin <1.5-3xULN postpone and reassess (if liver toxicity persists for more than 3 weeks discontinue treatment).
AST/ALT 20xULN and bilirubin >3xULN discontinue
Elevation of creatinine ≤2.5xULN give 100% dose
Elevation of creatinine ≥2.6xULN postpone dosing and reassess 1 week later (if after a 2 week delay the creatinine is still elevated by ≥2.6ULN discontinue treatment).

INVESTIGATIONS
Routine Blood test
1) Blood results required before chemotherapy administration

<table>
<thead>
<tr>
<th>Test</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL</td>
<td>≥10 &lt; 10</td>
</tr>
<tr>
<td>Plt x 10⁹/L</td>
<td>≥100 &lt; 100</td>
</tr>
<tr>
<td>Neutrophils x 10⁹/L</td>
<td>≥1.5 &lt; 1.5</td>
</tr>
</tbody>
</table>

2) Non urgent blood tests. Tests relating to disease response/progression
CONCURRENT MEDICATION
Caution with drugs affecting CYP 3A4 isoenzyme (e.g. omeprazole, fluoxetine, erythromycin, amiodarone, carbamazepine, phenytoin)
Consider concomitant laxatives particularly in patients with a history of constipation or those receiving opioid analgesics.

ANTIEMETIC POLICY
Minimal emetic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
VINORELBINE 25 (28 day)

NICE guidance – www.nice.org.uk
Vinorelbine monotherapy is not recommended as a first line treatment for advanced breast cancer. Vinorelbine monotherapy is recommended as one option for second line or later therapy for the treatment of advanced breast cancer when anthracycline-based regimens have failed or are unsuitable.

DRUG REGIMEN
Day 1 VINORELBINE 25mg/m² IV infusion in 50ml sodium chloride 0.9% over 10 minutes
Day 8 VINORELBINE 25mg/m² IV infusion in 50ml sodium chloride 0.9% over 10 minutes
Day 15 VINORELBINE 25mg/m² IV infusion in 50ml sodium chloride 0.9% over 10 minutes

Cycle Frequency: Every 28 days for 6 cycles subject to tolerance and response

NB: Day 15 sometimes omitted

DOSE MODIFICATIONS
Previous neutropenic sepsis, discuss with Consultant or Registrar
AST/ALT ≤5xULN and bilirubin <1.55xULN give 100% dose
AST/ALT 5.1-20xULN and bilirubin <1.5-3xULN postpone and reassess (if liver toxicity persists for more than 3 weeks discontinue treatment).
AST/ALT 20xULN and bilirubin >3xULN discontinue
Elevation of creatinine ≤2.5xULN give 100% dose
Elevation of creatinine ≥2.6xULN postpone dosing and reassess 1 week later (if after a 2 week delay the creatinine is still elevated by ≥2.6ULN discontinue treatment).

INVESTIGATIONS
Routine Blood test
1) Blood results required before chemotherapy administration
   
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb x g/dL</td>
<td>≥10</td>
</tr>
<tr>
<td>Plt x 10⁹/L</td>
<td>≥100</td>
</tr>
<tr>
<td>Neutrophils x 10⁹/L</td>
<td>≥1.5</td>
</tr>
</tbody>
</table>

2) Non urgent blood tests. Tests relating to disease response/progression

CONCURRENT MEDICATION
Caution with drugs affecting CYP 3A4 isoenzyme (e.g. omeprazole, fluoxetine, erythromycin, amiodarone, carbamazepine, phenytoin)
Consider concomitant laxatives particularly in patients with a history of constipation or those receiving opioid analgesics.
ANTIEMETIC POLICY
Minimal emetic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Vinorelbine
25 4 weekly

Breast TSSG Chair Authorisation:
Date:

Page 2 of 2
Published: March 2012
Review: March 2014
Version 3.2
VINORELBINE oral (28 day)

For use in individually funded patients

NICE guidance – www.nice.org.uk
Vinorelbine monotherapy is not recommended as a first line treatment for advanced breast cancer. Vinorelbine monotherapy is recommended as one option for second line or later therapy for the treatment of advanced breast cancer when anthracycline based regimens have failed or are unsuitable.

DRUG REGIMEN
Cycle 1
Day 1 VINORELBINE 60mg/m² PO
Day 8 VINORELBINE 60mg/m² PO
Day 15 VINORELBINE 60mg/m² PO

Cycle 2 onwards (if cycle 1 tolerated see dose modifications)
Day 1 VINORELBINE 80mg/m² PO
Day 8 VINORELBINE 80mg/m² PO
Day 15 VINORELBINE 80mg/m² PO

Cycle Frequency: Every 28 days for 6 cycles subject to tolerance and response

NB: total dose should never exceed 160mg per week. Capsules available in 20mg and 30mg strengths and must be stored in fridge.

DOSE MODIFICATIONS
Previous neutropenic sepsis, discuss with Consultant or Registrar.

From cycle 2, consider increasing dose to 80mg/m² days 1,8,15 except for patients in whom neutrophils dropped <0.5x10⁹/L once or patients in whom neutrophils dropped between 0.5-x10⁹/L during first cycle.

For any administration at 80mg/m², if neutrophils <0.5x10⁹/L, administration should be delayed until recovery and the dose reduced to 60mg/m² for the next three administrations. See product literature for dose re-escalation guidelines.

No prospective study is available in order to establish guidelines for the dose reduction of Vinorelbine capsules in hepatic impairment.

If there is significant hepatic impairment the dose of Vinorelbine soft capsules should be reduced. In patients with massive liver metastases (i.e. >75% of liver volume replaced by the tumour) it is empirically suggested that the dose be reduced by 25% and the haematological parameters closely monitored.
INVESTIGATIONS
Routine Blood test
1) Blood results required before chemotherapy administration
   - **Give**
   - **Discuss**
   - **Hb x g/dL**
     - ≥10
     - < 10
   - **Plt x 10⁹/L**
     - ≥100
     - < 100
   - **Neutrophils x 10⁹/L**
     - ≥1.5
     - < 1.5

2) Non urgent blood tests.
Tests relating to disease response/progression

CONCURRENT MEDICATION
Caution with drugs affecting CYP 3A4 isoenzyme (e.g., omeprazole, fluoxetine, erythromycin, amiodarone, carbamazepine, phenytoin)

Consider concomitant laxatives particularly in patients with a history of constipation or those receiving opioid analgesics.

ANTIEMETIC POLICY
Moderate emetic risk

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
## Common Toxicity Criteria

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergic</td>
<td>None</td>
<td>Transient rash, drug fever ≤38°C (100.4°F)</td>
<td>Urticaria, drug fever ≥38°C (100.4°F) and/or asymptomatic bronchospasm</td>
<td>Symptomatic bronchospasm requiring parenteral medication(s) with or without urticaria; allergy related oedema / angioedema</td>
<td>Anaphylaxis</td>
</tr>
<tr>
<td>Alopecia</td>
<td>Normal</td>
<td>Mild hair loss</td>
<td>Pronounced hair loss</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Anorexia</td>
<td>None</td>
<td>Loss of appetite</td>
<td>Oral intake significantly decreased</td>
<td>Requiring IV fluids</td>
<td>Requiring feeding tube or parenteral nutrition</td>
</tr>
<tr>
<td>Blood counts Neutrophils</td>
<td>Within normal limits</td>
<td>1.5x10⁹/L - normal</td>
<td>1.0-1.4x10⁹/L</td>
<td>0.5-0.9x10⁹/L</td>
<td>&lt;0.5x10⁹/L</td>
</tr>
<tr>
<td>Blood counts Haemoglobin</td>
<td>Within normal limits</td>
<td>10.0g/dl – normal</td>
<td>8.0 – 9.9g/dl</td>
<td>6.5-7.9g/dl</td>
<td>&lt;6.5g/dl</td>
</tr>
<tr>
<td>Blood counts Platelets</td>
<td>Within normal limits</td>
<td>75x10⁹/L - normal</td>
<td>50-74x10⁹/L</td>
<td>10-49x10⁹/L</td>
<td>&lt;10x10⁹/L</td>
</tr>
<tr>
<td>Blood counts White blood count</td>
<td>Within normal limits</td>
<td>3.0x10⁹/L - normal</td>
<td>2.0-2.9x10⁹/L</td>
<td>1.0-1.9x10⁹/L</td>
<td>&lt;1.0x10⁹/L</td>
</tr>
<tr>
<td>Diarrhoea (patients with colostomy)</td>
<td>None</td>
<td>Mild increase in loose, watery colostomy output compared with pre-treatment</td>
<td>Moderate increase in loose, watery colostomy output compared with pre-treatment, but not interfering with normal activity</td>
<td>Severe increase in loose, watery colostomy output compared with pre-treatment, interfering with normal activity</td>
<td>Physiologic consequences requiring intensive care, or haemodynamic collapse</td>
</tr>
<tr>
<td>Diarrhoea (patients without colostomy)</td>
<td>None</td>
<td>Increase of &lt;4 stools/day over pre-treatment</td>
<td>Increase of 4-6 stools/day, or nocturnal stools</td>
<td>Increase of 7-9 stools/day, or incontinence; or need for parenteral support for dehydration</td>
<td>Increase of &gt; 10 stools/day or bloody diarrhoea or parenteral support needed</td>
</tr>
<tr>
<td>Hand-foot skin reaction</td>
<td>None</td>
<td>Skin changes or dermatitis without pain</td>
<td>Skin changes with pain, not interfering with function</td>
<td>Skin changes with pain, interfering with function</td>
<td>-</td>
</tr>
<tr>
<td>Hepatic – alk phos</td>
<td>UNL</td>
<td>&gt;ULN – 2.5x ULN</td>
<td>&gt;2.5 – 5.0xULN</td>
<td>5.0 – 20.0xULN</td>
<td>&gt;20.0XULN</td>
</tr>
<tr>
<td>Hepatic – bilirubin</td>
<td>UNL</td>
<td>&gt;ULN – 1.5x ULN</td>
<td>&gt;1.5 – 3.0xULN</td>
<td>3.0 – 10.0xULN</td>
<td>&gt;10.0XULN</td>
</tr>
<tr>
<td>Symptom</td>
<td>None</td>
<td>Increased fatigue over baseline, but not altering normal activities</td>
<td>Moderate (decrease in performance status by level 1) or causing difficulty performing some activities</td>
<td>Severe (decrease in performance status by ≥2 levels), or loss of ability to perform some activities</td>
<td>Bedridden or disabling</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-----------------------</td>
<td>------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------</td>
<td>------------------------</td>
</tr>
<tr>
<td>Lethargy</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
<td>Bedridden or disabling</td>
</tr>
<tr>
<td>Nausea</td>
<td>None</td>
<td>Able to eat</td>
<td>Oral intake significantly decreased</td>
<td>No significant intake, requiring IV fluids</td>
<td>-</td>
</tr>
<tr>
<td>Neuropathy - motor</td>
<td>Normal</td>
<td>Subjective weakness but no objective findings</td>
<td>Mild objective weakness interfering with function, but not interfering with activities of daily living</td>
<td>Objective weakness interfering with activities of daily living</td>
<td>Paralysis</td>
</tr>
<tr>
<td>Neuropathy - sensory</td>
<td>Normal</td>
<td>Loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function</td>
<td>Objective sensory loss or paresthesia (including tingling), interfering with function, but not interfering with activities of daily living</td>
<td>Sensory loss of paresthesia interfering with activities of daily living</td>
<td>Permanent sensory loss that interferes with function</td>
</tr>
<tr>
<td>Pain</td>
<td>None</td>
<td>Mild pain not interfering with function</td>
<td>Moderate pain: pain or analgesics interfering with function but not interfering with activities of daily living</td>
<td>Severe pain: pain or analgesics severely interfering with activities of daily living</td>
<td>Disabling</td>
</tr>
<tr>
<td>Stomatitis / mucositis</td>
<td>None</td>
<td>Painless ulcers, erythema or mild soreness</td>
<td>Painful erythema, oedema or ulcers but can eat or swallow</td>
<td>Painful erythema oedema, or ulcers requiring IV hydration</td>
<td>Severe ulceration or requires parenteral or enteral nutritional support or prophylactic intubation</td>
</tr>
<tr>
<td>Vomiting</td>
<td>None</td>
<td>1 episode in 24 hours</td>
<td>2-5 episodes in 24 hours</td>
<td>≥6 episodes in 24 hours, or need for IV fluids</td>
<td>Requiring parenteral nutrition, or physiological consequences requiring intensive care; haemodynamic collapse</td>
</tr>
</tbody>
</table>