**Indication**
Palliative therapy for advanced breast cancer where initial chemotherapy with an anthracycline has failed or is inappropriate.

(NICE CG81)

**ICD-10 codes**
Codes pre-fixed with C50.

**Regimen details**

**21 day cycle**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, 8, 15</td>
<td>Paclitaxel</td>
<td>80*mg/m²</td>
<td>IV infusion</td>
</tr>
</tbody>
</table>

**28 day cycle**

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, 8, 15</td>
<td>Paclitaxel</td>
<td>90*mg/m²</td>
<td>IV infusion</td>
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</tbody>
</table>

No treatment on day 22

Dose may vary from 60-100mg/m² based on performance status.

**Cycle frequency**
21 or 28 days

**Number of cycles**
6 cycles

**Administration**
Paclitaxel is administered in a 250-500mL sodium chloride 0.9% non-PVC infusion bag with a 0.22 micron in-line filter over 1 hour.

Blood pressure and pulse should be monitored regularly (e.g. every 30 minutes) during paclitaxel infusion.

Patients should be observed closely for hypersensitivity reactions, particularly during the first and second infusions. Hypersensitivity reactions may occur within a few minutes following the initiation of the infusion of paclitaxel. Facilities for the treatment of hypotension and bronchospasm must be available.

If hypersensitivity reactions occur, minor symptoms such as flushing or localised cutaneous reactions do not require discontinuation of therapy. The infusion may be temporarily interrupted and when symptoms improve restarted at a slower infusion rate. Chlorphenamine 10mg IV may be administered. Severe reactions, such as hypotension, bronchospasm or generalised rash/erythema require immediate discontinuation of paclitaxel and appropriate therapy should be initiated.

**Pre-medication**
30 minutes prior to each infusion:
Ranitidine 50mg IV slow bolus  
Chlorphenamine 10mg IV slow bolus  
Dexamethasone 8mg IV slow bolus

**Emetogenicity**  
This regimen has moderate emetic potential.

**Additional supportive medication**  
Mouthwashes as per local policy  
H₂ antagonist or PPI, if required, as per local policy

**Extravasation**  
Paclitaxel – vesicant (Group5)

### Investigations – pre first cycle

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Validity period (or as per local practice)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBC</td>
<td>14 days</td>
</tr>
<tr>
<td>U+E (including creatinine)</td>
<td>14 days</td>
</tr>
<tr>
<td>LFTs</td>
<td>14 days</td>
</tr>
</tbody>
</table>

### Investigations – pre subsequent cycles

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Validity period (or as per local practice)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBC</td>
<td>24 hours – prior to each dose</td>
</tr>
<tr>
<td>U+E (including creatinine)</td>
<td>72 hours – prior to day 1 only</td>
</tr>
<tr>
<td>LFTs</td>
<td>72 hours – prior to day 1 only</td>
</tr>
</tbody>
</table>

**Standard limits for administration to go ahead**  
If blood results not within range, authorisation to administer must be given by prescriber/consultant

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophils</td>
<td>$\geq 1.0 \times 10^9$/L</td>
</tr>
<tr>
<td>Platelets</td>
<td>$\geq 100 \times 10^9$/L</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>$&lt; 1.5 \times$ ULN</td>
</tr>
<tr>
<td>AST/ALT</td>
<td>$&lt; 5 \times$ ULN</td>
</tr>
</tbody>
</table>

**Dose modifications**

- **Haematological toxicity**  
  If neutrophils $< 1.0 \times 10^9$/L and/or platelets $< 100 \times 10^9$/L delay for 1 week then resume at 100% dose. If delayed for $> 1$ week discuss with consultant.

  In the case of febrile neutropenia (neutrophils $< 0.5 \times 10^9$/L and fever $> 38.5^\circ$C requiring IV antibiotics) reduce paclitaxel to 60mg/m² for all future doses.

- **Renal impairment**  
  No dose modifications required.

- **Hepatic impairment**  
  Paclitaxel is not recommended in severe hepatic impairment. If bilirubin $< 1.5 \times$ ULN and AST/ALT $< 5 \times$ ULN proceed with 100% dose. For more severe hepatic impairment, treatment may only proceed on consultant’s decision, at a reduced dose with weekly monitoring of LFTs.
### Other toxicities

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Definition</th>
<th>Paclitaxel dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuropathy</td>
<td>Grade 2</td>
<td>Reduce to a maximum of 70mg/m² for all subsequent doses.</td>
</tr>
<tr>
<td></td>
<td>Grade ≥ 3</td>
<td>Discontinue</td>
</tr>
</tbody>
</table>

For all other grade ≥ 2 toxicities (except alopecia) withhold until grade ≤ 1 and continue with 70mg/m² dose. If delayed for > 1 week, discuss with consultant.

For any grade 4 toxicity (except alopecia) withhold and discuss with consultant.

**Adverse effects** - for full details consult product literature/ reference texts

- **Rare or serious side effects**
  - Myelosuppression
  - Infertility
  - Teratogenicity
  - Hypersensitivity reactions
  - Pulmonary fibrosis
  - Electrolyte disturbances
  - Arrhythmias
  - Cardiac failure

- **Frequently occurring side effects**
  - Nausea and vomiting
  - Mucositis, stomatitis
  - Myelosuppression
  - Diarrhoea, constipation
  - Peripheral neuropathy
  - Oedema
  - Phlebitis
  - Myalgia, arthralgia
  - Alopecia
  - Fatigue

- **Other side effects**
  - Taste changes
  - Headache
  - Abdominal pain

**Significant drug interactions** – for full details consult product literature/ reference texts

- **Warfarin/coumarin anticoagulants**: increased or fluctuating anticoagulant effects. Avoid if possible, consider switching patient to a low molecular weight heparin during treatment or if the patient continues taking an oral anticoagulant monitor the INR at least once a week and adjust dose accordingly.

- **Clozapine**: increased risk of agranulocytosis

- **Paclitaxel** is a CYP 2C8/9 and CYP 3A4 substrate. Drug levels may be increased by inhibitors of these enzymes and decreased by inducers of these enzymes.

**Additional comments**

Nil
References

- Summary of Product Characteristics Paclitaxel (Hospira) accessed 29 October 2014 via www.medicines.org.uk
- Verrill, M., et al –. Abstract only ASCO 2007 LBA1005

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