PACLITAXEL weekly PERTUZUMAB (Perjeta) TRASTUZUMAB IV

INDICATION (ICD10) C50
Adjuvant HER 2+ve patient who is contraindicated to docetaxel following on from anthracycline containing treatment (Eg in EC-docetaxel) and meets all Blueteq criteria.
(Weekly schedule is unlicensed treatment).

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required.
(www.england.nhs.uk/publication/national-cancer-drugs-fund-list/)
Pertuzumab in combination with intravenous trastuzumab and chemotherapy as adjuvant therapy for axillary node positive HER2-positive early breast cancer and with NO preceding neoadjuvant chemotherapy in combination with pertuzumab and trastuzumab (PER3) where the following criteria have been met:
2. Histologically documented breast cancer which is HER2 3+ by immunohistochemistry and/or has a ratio of ≥2.0 by in situ hybridisation.
3. Early breast cancer and this has been adequately excised.
4. Pathologically confirmed axillary lymph node involvement. Pertuzumab in combination with trastuzumab as adjuvant treatment is only NICE-recommended and commissioned in patients with pathologically documented axillary lymph node involvement.
5. Due to commence adjuvant chemotherapy in combination with pertuzumab and trastuzumab and will receive one of the standard adjuvant anthracycline- and/or taxane-based chemotherapy regimens as set out in pertuzumab’s Summary of Product Characteristics.
6. 3-4 cycles of EC followed by 3-4 cycles of docetaxel (or 12 cycles of weekly paclitaxel). If a patient has a severe allergic reaction to the docetaxel part of the treatment combination, the patient can be switched to a trial of weekly paclitaxel. Pertuzumab and trastuzumab should commence with the first taxane cycle. Pertuzumab and trastuzumab are not commissioned in combination with other adjuvant chemotherapy regimens.
7. A maximum of 18 cycles of pertuzumab plus trastuzumab will be administered as adjuvant treatment.
8. The trastuzumab will be given intravenously and that best value intravenous trastuzumab is being used. Subcutaneous trastuzumab is not commissioned in combination with pertuzumab.
9. ECOG performance status of 0 or 1.
10. The pre-treatment left ventricular ejection fraction was ≥55% and if anthracyclines were given that the LVEF was ≥50% after completion of the anthracycline component of the adjuvant chemotherapy.
11. Treatment breaks of up to 6 weeks are allowed, but solely to allow toxicities to settle
12. Pertuzumab will be otherwise used as set out in its Summary of Product Characteristics.
### REGIMEN

Trastuzumab or pertuzumab can be given in any order (but wait 30 minutes after pertuzumab before administering other SACT agents)

#### Cycle 1

**Day 1**

- Premedication 30 minutes prior to infusion:
  - Dexamethasone 8mg IV bolus
  - Ranitidine 50mg IV bolus
  - Chlorphenamine 10mg IV bolus
  - **PACLITAXEL** 80mg/m² in 250ml* sodium chloride 0.9% infusion over 60 minutes
  - **TRASTUZUMAB** 8mg/kg in 250ml sodium chloride 0.9% IV infusion
  - **PERTUZUMAB** 840mg in 250ml sodium chloride 0.9% IV infusion

**Days 8 and 15**

- Premedication 30 minutes prior to infusion:
  - Dexamethasone 8mg IV bolus
  - Ranitidine 50mg IV bolus
  - Chlorphenamine 10mg IV bolus
  - **PACLITAXEL** 80mg/m² in 250ml* sodium chloride 0.9% infusion over 60 minutes

#### Cycles 2 to 4

**Day 1**

- Premedication 30 minutes prior to infusion:
  - Dexamethasone 8mg IV bolus
  - Ranitidine 50mg IV bolus
  - Chlorphenamine 10mg IV bolus
  - **PACLITAXEL** 80mg/m² in 250ml* sodium chloride 0.9% infusion over 60 minutes
  - **TRASTUZUMAB** 6mg/kg in 250ml sodium chloride 0.9% IV infusion
  - **PERTUZUMAB** 420mg in 250ml sodium chloride 0.9% IV infusion

**Days 8 and 15**

- Premedication 30 minutes prior to infusion:
  - Dexamethasone 8mg IV bolus
  - Ranitidine 50mg IV bolus
  - Chlorphenamine 10mg IV bolus
  - **PACLITAXEL** 80mg/m² in 250ml* sodium chloride 0.9% infusion over 60 minutes

* doses 162mg to 600mg in 500ml sodium chloride 0.9%

#### Cycles 5 to 18

**Day 1**

- **TRASTUZUMAB** 6mg/kg in 250ml sodium chloride 0.9% IV infusion
- **PERTUZUMAB** 420mg in 250ml sodium chloride 0.9% IV infusion

NB Trastuzumab SPC states patients need to be monitored for 6 hours after the start of the first dose and 2 hours after the start of subsequent doses.

Cycle 1 - administer trastuzumab over 90 minutes. Monitor for 3.5 hours post start of infusion (2 hours after completion) of the first dose.

Subsequent cycles - if the initial loading dose was well tolerated (no signs of hypersensitivity), the 2nd dose can be administered as a 30 minute infusion (otherwise to continue to be administered over 90 minutes), and subsequent infusions can be administered over 30 minutes.

If the first cycle was well tolerated, following the 2nd and 3rd cycles patients should be observed on the ward / day unit for 30 minutes after the completion of trastuzumab infusion.

If the 2nd and 3rd cycles were well tolerated, after the 4th and subsequent cycles patients do not need to be observed following completion of trastuzumab infusion.

Patients should be warned of the possibility of delayed reactions and instructed to seek medical advice immediately should this occur.
CYCLE FREQUENCY AND NUMBER OF CYCLES
Combination every 21 days cycles 1 to 4
Pertuzumab and Trastuzumab every 21 day cycles 5 to 18

ANTI-EMETICS
Low risk days 1, 8 and 15 cycles 1 to 4
Minimal risk day 1 cycles 5 to 18

CONCURRENT MEDICATION REQUIRED

<table>
<thead>
<tr>
<th>Medication</th>
<th>Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paclitaxel</td>
<td>Ensure premedication given before paclitaxel</td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>Infusion related chills and/or fevers – treat with paracetamol and chlorphenamine.</td>
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</tbody>
</table>

EXTRAVASATION AND TYPE OF LINE / FILTERS
Paclitaxel – vesicant
Pertuzumab - neutral
Trastuzumab - neutral

Administer paclitaxel via polyethylene lined administration set with ≤0.22micron filter
Central line

INVESTIGATIONS
Blood results required before SACT administration
FBC, U&E and LFTs every week cycles 1 to 6 then every cycle
Neutrophils x 10^9/L ≥1.0 (adjuvant or neoadjuvant use)
Platelets x 10^9/L ≥100
Baseline weight and every cycle cycles 1 to 4 then 3 monthly weight.
Monitor cardiac function according to network guidelines

MAIN TOXICITES AND ADVERSE REACTIONS

<table>
<thead>
<tr>
<th>Medication</th>
<th>Reaction</th>
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<tbody>
<tr>
<td>Paclitaxel</td>
<td>(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.</td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>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.</td>
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</tbody>
</table>
INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS
(not exhaustive list check SPC/BNF/Stockleys)

| Paclitaxel       | DOACs to be used with caution, need dose modifications or to be avoided eg apixaban  
|                 | Clopidogrel interacts with paclitaxel, potentially increasing the concentration of paclitaxel.  
|                 | Paclitaxel is catalysed, by cytochrome P450 isoenzymes CYP2C8 and CYP3A4.  
|                 | inhibitors (e.g. erythromycin, fluoxetine, gemfibrozil) use with caution. inducers (e.g. rifampicin, carbamazepine, phenytoin, phenobarbital, efavirenz, nevirapine) use with caution. |

DOSE MODIFICATIONS
Delay more than 6 weeks since last dose
The 840 mg loading dose of pertuzumab should be re-administered as a 60 minute infusion, followed by a maintenance dose of 420 mg IV administered every 3 weeks thereafter. The loading dose of 8 mg/kg of trastuzumab IV should be re-administered over approximately 90 minutes, followed by a maintenance dose of 6 mg/kg IV administered every 3 weeks thereafter.

Haematological
Pertuzumab
Dose reductions are not recommended for Pertuzumab.
Patients may continue therapy during periods of reversible chemotherapy-induced myelosuppression but they should be monitored carefully for complications of neutropenia during this time.
If trastuzumab treatment is discontinued, treatment with Pertuzumab should be discontinued.

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

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

Trastuzumab and pertuzumab
Continuation and discontinuation of trastuzumab based on interval LVEF assessment as per network guidelines

Hepatic impairment
Paclitaxel
In the absence of Gilbert's syndrome:

| Bilirubin <26 micromol/L | give 80mg/m² |
| Bilirubin 27-51micromol/L | give 65mg/m² |
| Bilirubin >51micromol/L | withhold |
REFERENCES