

## **PACLITAXEL weekly PERTUZUMAB / TRASTUZUMAB (Phesgo) SC (following completion of anthracycline component ie 3-4 cycles EC)**

### **INDICATION (ICD10) C50**

*Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/)* (PER3), (PER2b), (PER2a)

1. Pertuzumab in combination with intravenous trastuzumab and chemotherapy as adjuvant therapy for axillary node positive HER2-positive (HER2 3+), adequately excised early breast cancer and with NO preceding neoadjuvant chemotherapy in combination with pertuzumab and trastuzumab, following 3-4 cycles of EC. PS 0 or 1. (TA569)
2. Neoadjuvant pertuzumab in patients who are HER2 3+ NODE NEGATIVE or of UNKNOWN NODAL STATUS for previously untreated neoadjuvant treatment of locally advanced, inflammatory or early breast cancer at high risk of recurrence (stage T2-T4b and M0 disease) in combination with taxane chemotherapy, following 3-4 cycles of EC. (TA424)
3. Neoadjuvant pertuzumab in HER2 3+ NODE POSITIVE patients for previously untreated neoadjuvant treatment of locally advanced, inflammatory or early breast cancer at high risk of recurrence (stage T2-T4b and M0 disease) in combination with taxane chemotherapy, following 3-4 cycles of EC. (TA424)

### **REGIMEN**

When given in combination with a taxane on the same day the pertuzumab and trastuzumab should be administered 30 minutes before the taxane.

#### **Cycle 1**

Day 1 Premedication 30 minutes prior to infusion:  
 Dexamethasone 8mg IV bolus  
 Chlorphenamine 10mg IV bolus  
 PACLITAXEL 80mg/m<sup>2</sup> in 250ml\* sodium chloride 0.9% infusion over 60 minutes  
 \*\*PERTUZUMAB with TRASTUZUMAB 1800mg SC over 8 minutes

Days 8 and 15 Premedication 30 minutes prior to infusion:  
 Dexamethasone 8mg IV bolus  
 Chlorphenamine 10mg IV bolus  
 PACLITAXEL 80mg/m<sup>2</sup> 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  
 Chlorphenamine 10mg IV bolus  
 PACLITAXEL 80mg/m<sup>2</sup> in 250ml\* sodium chloride 0.9% infusion over 60 minutes  
 \*\*PERTUZUMAB with TRASTUZUMAB 1200mg SC over 5 minutes

Days 8 and 15 Premedication 30 minutes prior to infusion:  
 Dexamethasone 8mg IV bolus  
 Chlorphenamine 10mg IV bolus  
 PACLITAXEL 80mg/m<sup>2</sup> 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 \*\*PERTUZUMAB with TRASTUZUMAB 1200mg SC over 5 minutes

\*\*For patients unable to receive SC pertuzumab / trastuzumab (phesgo) see the pertuzumab trastuzumab IV substitution regimen for IV pertuzumab plus IV trastuzumab doses, observation times etc.

Pertuzumab / Trastuzumab loading dose - observation time post injection 30 minutes

Pertuzumab / Trastuzumab maintenance doses - observation time post injection 15 minutes

### CYCLE FREQUENCY AND NUMBER OF CYCLES

Combination every 21 days cycles 1 to 4

Pertuzumab with Trastuzumab every 21 days 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

Paclitaxel	Ensure premedication given before paclitaxel
Pertuzumab with Trastuzumab	Infusion related chills and/or fevers – treat with paracetamol and chlorphenamine.

### EXTRAVASATION AND TYPE OF LINE / FILTERS

Paclitaxel – vesicant

Administer paclitaxel via polyethylene lined administration set with  $\leq 0.22$ micron 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  $10^9/L \geq 1.0$  (0.8-1.0 on the day of chemo go ahead with GCSF support as per local policy) (adjuvant or neoadjuvant use)

Platelets x  $10^9/L \geq 100$

Baseline weight and every cycle cycles 1 to 4 then 3 monthly weight.

Monitor cardiac function according to network guidelines. Baseline LVEF greater than or equal to 55% or if anthracyclines were given that the LVEF was greater than or equal to 50% after completion of the anthracycline component of the adjuvant chemotherapy.

## MAIN TOXICITIES AND ADVERSE REACTIONS

Paclitaxel	(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.
Pertuzumab with Trastuzumab	Cardiotoxicity - monitor cardiac function. Injection related chills, fevers or headache, slow the rate of injection or pause and appropriate medical therapies administered (Treatment including oxygen, beta agonists, antihistamines, rapid intravenous fluids and antipyretics may also help alleviate systemic symptoms.). For severe injection related reactions discontinue permanently. Other symptoms may include nausea, hypertension, vomiting, pain, rigors, headache, cough, dizziness, rash, and asthenia. Febrile neutropenia, diarrhea, pulmonary events Cardiomyopathy: Pertuzumab with trastuzumab administration can result in subclinical and clinical cardiac failure manifesting as CHF, and decreased LVEF, with greatest risk when administered concurrently with anthracyclines. Evaluate cardiac function prior to and during treatment. Discontinue pertuzumab with trastuzumab for cardiomyopathy.

## 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.
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## DOSE MODIFICATIONS

Pertuzumab with trastuzumab

Delay more than 6 weeks since last dose

The loading dose of pertuzumab with trastuzumab 1800mg SC (equivalent to pertuzumab 1200mg and trastuzumab 600mg (1200/600mg vial)) should be readministered for 1 dose then followed by maintenance doses of pertuzumab with trastuzumab 1200mg SC (equivalent to pertuzumab 600mg and trastuzumab 600mg (600/600mg vial)).

## Non-haematological

Paclitaxel

If patient complains of tinnitus, tingling of fingers and/or toes or motor weakness

discuss with Consultant or Registrar before administration

If grade  $\geq 2$  neuropathy, consider giving 75% paclitaxel dose

If grade  $> 3$  peripheral neuropathy is  $>$  grade 3 omit further paclitaxel

Pertuzumab with Trastuzumab

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

## Hepatic impairment

Paclitaxel

In the absence of Gilbert's syndrome:

Transaminase <10xULN and bilirubin ≤1.25xULN	no dose reduction
Transaminase <10xULN and bilirubin 1.26-2xULN	clinician discretion
Transaminase <10xULN and bilirubin 2.01-5xULN	clinician discretion
Transaminase ≥10xULN or bilirubin >5xULN	contraindicated

## REFERENCES

1. Andrew D. Seidman, Donald Berry, Constance Cirrincione, Lyndsay Harris, Hyman Muss, P. Kelly Marcom, Grandella Gipson, Harold Burstein, Diana Lake, Charles L. Shapiro, Peter Ungaro, Larry Norton, Eric Winer and Clifford Hudis. JCO 2008. Randomized Phase III Trial of Weekly Compared With Every-3-Weeks Paclitaxel for Metastatic Breast Cancer, With Trastuzumab for all HER-2 Overexpressors and Random Assignment to Trastuzumab or Not in HER-2 Nonoverexpressors: Final Results of Cancer and Leukemia Group B Protocol 9840
2. Joseph A. Sparano, M.D., Molin Wang, Ph.D., Silvana Martino, D.O., Vicky Jones, M.D., Edith A. Perez, M.D., Tom Saphner, M.D., Antonio C. Wolff, M.D., George W. Sledge, Jr., M.D., William C. Wood, M.D., and Nancy E. Davidson, M.D. N Engl J Med. 2008 Apr 17; 358(16): 1663–1671. doi: 10.1056/NEJMoa0707056 Weekly Paclitaxel in the Adjuvant Treatment of Breast Cancer