Pertuzumab and Trastuzumab (Phesgo®) and DOCEtaxel Therapy - 21 day cycle

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
Pertuzumab/ trastuzumab (Phesgo®) is indicated in combination with DOCEtaxel in adult patients with HER2-positive metastatic or locally recurrent unresectable breast cancer, who have not received previous anti- HER2 therapy or chemotherapy for their metastatic disease.	C50	00796a	Pertuzumab/Trastuzumab (Phesgo®): ODMS 20/12/2022 DOCEtaxel: N/A

* This is for post 2012 indications only.

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Treatment is administered every 21 days in responding patients until disease progression or unacceptable toxicity develops.

Facilities to treat anaphylaxis MUST be present when systemic anti-cancer therapy (SACT) is administered.

Cycle 1: Pertuzumab and trastuzumab (Phesgo ®) loading dose

Order of Admin	Day	Drug	Dose	Route	Diluent & Rate
1	1	Pertuzumab/ Trastuzumab (Phesgo®)	1200mg/600mg	SC Observe for 30 minutes post injection[a]	Over 8 minutes
2	1	DOCEtaxel[b]	75mg/m^2	IV infusion	250mL 0.9% NaCl over 60 minutes[c]
[a]Patients should be observed for injection-related reactions and hypersensitivity reactions. Observation period should start following administration of Phesgo® and be completed prior to any subsequent administration of chemotherapy. Any deviation should be noted in local policies.					
[b]Primary prophylaxis with G-CSF should be considered to reduce the risk of neutropenic complications(See Adverse Effects/Regimen Specific Complications)					
[c]75-185mg dose use 250mL infusion bag. For doses> 185mg use 500mL infusion bag Use non-PVC infusion equipment					

Cycle 2 and subsequent cycles

Order of Admin	Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	1	Pertuzumab/ Trastuzumab (Phesgo®)	600mg/600mg	SC Observe for 15 minutes post injection[a]	Over 5 minutes if no adverse reactions	Every 21 days
2	1	DOCEtaxel[b]	[c]75mg/m^2	IV infusion	250ml 0.9% NaCl over 60 minutes[d]	Every 21 days for a minimum of 6 cycles
[a]Patients should be observed for injection-related reactions and hypersensitivity reactions. Observation period should start following administration of Phesgo® and be completed prior to any subsequent administration of chemotherapy. Any deviation should be noted in local policies.						
[b]Primary prophylaxis with G-CSF should be considered to reduce the risk of neutropenic complications (See Adverse Effects/Regimen Specific Complications)						
[c]The dose of DOCEtaxel may be escalated to 100 mg/m^2 on subsequent cycles if the initial dose is well tolerated.						
[d]75-185mg dose use 250mL infusion bag. For doses> 185mg use 500mL infusion bag Use non-PVC infusion bag.						

ELIGIBILITY:

- Indications as above
- HER2 overexpression or HER 2 gene amplification as determined by an accurate and validated assay. Please see *Recommendations on Reporting on HER2 Status in Breast Cancer Patients* here.
- ECOG status 0-1
- Patients should have a pre-treatment LVEF of ≥ 50%
- Adequate organ function

EXCLUSIONS:

- Hypersensitivity to pertuzumab, trastuzumab, DOCEtaxel, murine proteins or any of the excipients
- Clinically significant cardiac disease (history of symptomatic ventricular arrhythmias, congestive heart failure or myocardial infarction within previous 12 months)
- Patients experiencing dyspnoea at rest due to complications of advanced malignancy and comorbidities may be at increased risk of a fatal infusion reaction with trastuzumab
- Significant hepatic dysfunction, contraindicating DOCEtaxel
- Baseline neutrophil count < 1.5 x 10^9/L
- Pregnancy or breastfeeding

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist.

TESTS:

Baseline tests:

- Blood, renal and liver profile
- Cardiac function (LVEF using ECHO or MUGA scan)

Regular tests:

- FBC, renal and liver profile before each cycle
- MUGA scan or echocardiogram every 12 weeks. . Where there are signs of cardiac impairment four to eight weekly checks may be more appropriate.

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant

Pertuzumab/ trastuzumab (Phesgo®)

- None usually recommended. Doses are held or discontinued if unacceptable toxicity occurs. Please see Table 1 below for recommendations on resuming dosing with pertuzumab/trastuzumab (Phesgo®) after a dose delay or missed doses.
    - Doses are held or discontinued if unacceptable toxicity occurs.
    - Patient may continue to receive pertuzumab/trastuzumab (Phesgo®) if DOCEtaxel is discontinued due to toxicity or after 6-8 cycles and without evidence of disease progression.

Table 1: Delayed or missed doses for pertuzumab and trastuzumab (Phesgo®)

Time between two sequential infusions	Dose modification
<6 weeks	The maintenance dose of pertuzumab/trastuzumab **(**Phesgo®) 600 mg/600 mg should be administered as soon as possible. Thereafter, continue with the 3-weekly schedule.
≥6 weeks	A loading dose of pertuzumab/trastuzumab **(**Phesgo®) 1200 mg/600 mg should be re-administered followed by maintenance dose of pertuzumab/trastuzumab **(**Phesgo®) 600 mg/600 mg every 3 weeks thereafter.

Table 2: Switching from intravenous pertuzumab and trastuzumab administration to Phesgo®

Time since last dose	Dose of Phesgo®
<6 weeks	Administer as a maintenance dose of 600 mg pertuzumab/600 mg trastuzumab and every 3 weeks for subsequent administrations
≥6 weeks	Administered as a loading dose of 1200 mg pertuzumab/600 mg trastuzumab, followed by a maintenance dose of 600 mg pertuzumab/600 mg trastuzumab every 3 weeks for subsequent administrations.

Renal and Hepatic Impairment:

Table 3: Dose modification in renal and hepatic impairment

Drug	Renal Impairment	Hepatic Impairment
Pertuzumab/ trastuzumab (Phesgo®) [a]	Dose adjustments are not needed in patients with mild or moderate renal impairment. No dose recommendations can be made for patients with severe renal impairment because of the limited pharmacokinetic (PK) data available.	The safety and efficacy have not been studied in patients with hepatic impairment. Patients with hepatic impairment are unlikely to require dose adjustment. No specific dose adjustment are recommended.
DOCEtaxel [b]	No need for dose adjustment is expected Haemodialysis : no need for dose adjustment is expected	See Table 4 below
[a] Phesgo® (renal and hepatic – SPC) [b] DOCEtaxol (renal and hepatic – Giraud et al (2023))		

Table 4: Dose modification of DOCEtaxel in hepatic impairment.

AST Values		ALT Values		Alkaline Phosphatase Values		Bilirubin	Dose Modification
> 1.5–5 x ULN	AND/OR	> 1.5–5 x ULN	AND	> 2.5–5 x ULN	AND	Normal	Consider 75% of the original dose
> 5–10 x ULN	OR	> 5–10 x ULN	AND	< 6 x ULN	AND/OR	≤ 1–1.5 x ULN	Consider 50% of the original dose
> 10 x ULN	OR	> 10 x ULN	OR	> 6 x ULN	OR	> 1.5 x ULN	Not recommended

Management of adverse events:

Table 5: Dose modification schedule based on adverse events

Adverse reactions	Discontinue	Recommended dose modification
Pertuzumab/trastuzumab (Phesgo®)		
LVEF < 40% or 40-45% associated with ≥10% points below the pre-treatment value.		Withhold treatment with pertuzumab/trastuzumab (Phesgo®). Repeat LVEF within 3 weeks. No improvement or further decline discuss with consultant and consider referral to cardiology.
Symptomatic heart failure	Discontinue	
NCI-CTCAE Grade 4 hypersensitivity reactions	Discontinue	
DOCEtaxel		
Grade >2 peripheral neuropathy		Decrease dose of DOCEtaxel to 60mg/m^2. If the patient continues to experience these reactions at 60 mg/m^2, treatment with DOCEtaxel should be discontinued.
Grade 3 skin reaction		
Grade ≥3 stomatitis		DOCEtaxel will be reduced from 75 to 60 mg/m^2.

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

- As outlined in NCCP Classification Document for Systemic AntiCancer Therapy (SACT) Induced Nausea and Vomiting linked here

Pertuzumab/trastuzumab (Phesgo®): Minimal **(Refer to local policy)**
DOCEtaxel: Low (**Refer to local policy)**

Within NCIS regimens, antiemetics have been standardised by Medical Oncologists and Haemato-oncologists and information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) - link here
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) - link here

PREMEDICATIONS:

- **DOCEtaxel:** dexAMETHasone 8 mg PO twice daily for 3 days, starting one day prior to each DOCEtaxel administration unless contraindicated. Patient must receive minimum of 3 doses pre-treatment.
- Consideration may be given, at the discretion of the prescribing consultant, to the use of a single dose of dexAMETHasone 20mg IV immediately before chemotherapy where patients have missed taking the oral premedication dexamethasone as recommended by the manufacturer.

- **Pertuzumab/trastuzumab (Phesgo®):** Not usually required unless the patient has had a previous hypersensitivity. Paracetamol and antihistamine cover should be considered. Patient should be educated about the possibility of delayed infusion-related symptoms.

OTHER SUPPORTIVE CARE: No specific recommendations

ADVERSE EFFECTS

- Please refer to the relevant Summary of Product Characteristics (SmPC)

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for information.

REFERENCES:

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6. Chouhan et al. Single premedication dose of dexamethasone 20mg IV before docetaxel administration. J Oncol Pharm Practice 2010;17(3): 155–159
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11. Pertuzumab/Trastuzumab (Phesgo®) Summary of Product Characteristics. Accessed April 2024. Available here: https://www.ema.europa.eu/en/documents/product-information/phesgo-epar-product-information_en.pdf
12. DOCEtaxol (Taxotere®) Summary of Product Characteristics. Accessed April 2024.Available at :https://www.ema.europa.eu/en/documents/product-information/taxotere-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	20/12/2022		Prof Maccon Keane
2	10/08/2023	Updated emetogenic potential of pertuzumab/trastuzumab (Phesgo)	Prof Maccon Keane
3	27/05/2024	Updated eligibility section, regular testing section and renal and hepatic dose modifications section. Updated management of adverse events and drug interactions section.	Prof Maccon Keane
4	17/07/2024	Updated eligibility section. Updated emetogenic section with standard wording . Adverse Effects and Drug Interactions sections removed and replaced with standard wording.	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.