Pertuzumab/Trastuzumab (Phesgo®), PACLitaxel and CARBOplatin Therapy (TRAIN-2)

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
Neoadjuvant treatment of adult patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer at high risk of recurrence.	C50	00790a	Pertuzumab/Trastuzumab (Phesgo®): ODMS 20/12/2022 CARBOplatin and PACLitaxel: 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.

Pertuzumab/trastuzumab (Phesgo®), and CARBOplatin are administered on day 1 and PACLitaxel is administered on day 1 and 8 of a 21 day cycle for 6 cycles or until disease progression or unacceptable toxicity develops.

Following surgery, patients should be treated with adjuvant therapy (e.g. trastuzumab OR trastuzumab emtansine as appropriate) to complete 1 year of treatment.

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

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPSACTregimens

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

Admin. Order	Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	1	Pertuzumab/trastuzumab (Phesgo®)	1200mg/600mg	SC (Observe for 30 minutes post injection [a])	Over 8 minutes	Cycle 1 only
2	1, 8	PACLitaxel	80mg/m^2	IV infusion	250mL 0.9% NaCl over 60 minutes[b]	Cycle 1 only
3	1	CARBOplatin	AUC 6	IV infusion	500mL glucose 5% over 30 minutes	Cycle 1 only

[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] PACLitaxel must be supplied in non-PVC containers and administered using non-PVC giving sets and through an in-line 0.22µm filter with a microporous membrane. PACLitaxel should be diluted to a concentration of 0.3-1.2mg/mL.

Note: Administration volumes and fluids have been standardised to facilitate electronic prescribing system builds.

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPSACTregimens

Cycle 2-6

Admin. Order	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, 8	PACLitaxel	80mg/m^2	IV infusion	250mL 0.9% NaCl over 60 minutes[b]	Every 21 days
3	1	CARBOplatin	AUC 6	IV infusion	500mL glucose 5% over 30 minutes	Every 21 days
[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] PACLitaxel must be supplied in non-PVC containers and administered using non-PVC giving sets and through an in-line 0.22µm filter with a microporous membrane. PACLitaxel should be diluted to a concentration of 0.3-1.2mg/mL.						

Note: Administration volumes and fluids have been standardised to facilitate electronic prescribing system builds.

CARBOplatin dose:

The dose in mg of CARBOplatin to be administered is calculated as follows:

Dose (mg) = target AUC (mg/mL x minute) x (GFR mL/minute +25)

- **Measured GFR** (e.g. nuclear renogram) is preferred whenever feasible.
- **Estimation of GFR** (eGFR) can be done by using the Wright formula or using the Cockcroft and Gault formula to measure creatinine clearance.
- The GFR used to calculate the AUC dosing should not exceed 125mL/minute.
- For obese patients and those with a low serum creatinine, for example, due to low body weight or post-operative asthenia, the formulae may not give accurate results and measured GFR is recommended.

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPSACTregimens

- Where obesity (body mass index [BMI] ≥ 30 kg/m^2) or overweight (BMI 25-29.9) is likely to lead to an overestimate of GFR and isotope GFR is not available, the use of the adjusted ideal body weight for Cockcroft and Gault may be considered.
- Where serum creatinine is less than 63 micromol/L, the use of a creatinine value of 62 micromol/L or a steady pre-operative creatinine value may be considered.

- These comments do not substitute for the clinical judgement of a physician experienced in prescription of CARBOplatin.

WRIGHT FORMULA

There are two versions of the formula depending on how serum creatinine values are obtained, by the kinetic Jaffe method or the enzymatic method. The formula can be further adapted if covariant creatine kinase (CK) values are available (not shown).

1. *SCr measured using enzymatic assay.*

$$\text{GFR (mL/minute)} = \frac{(6230 - 32.8 \times \text{Age}) \times \text{BSA} \times (1 - 0.23 \times \text{Sex})}{\text{SCr (micromol/minute)}}$$

2. *SCr measured using Jaffe assay*

$$\text{GFR (mL/minute)} = \frac{(6580 - 38.8 \times \text{Age}) \times \text{BSA} \times (1 - 0.168 \times \textit{Sex})}{\text{SCr (micromol/minute)}}$$

Key: Sex = 1 if female, 0 if male; Age in years; BSA= DuBois BSA

COCKCROFT-GAULT FORMULA

$$\text{GFR (mL/minute)} = \frac{S \times (140 - \text{age in years}) \times \text{wt (kg)}}{\text{serum creatinine (micromol/L)}}$$

S = 1.04 for females and 1.23 for males

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPSACTregimens

ELIGIBILITY:

- Indications as above
- HER2 overexpression or HER2 gene amplification as determined by an accurate and validated assay. Please see *Recommendations on Reporting on HER2 Status in Breast Cancer Patients* here.
- ≥ 18 years
- ECOG status 0-1
- LVEF ≥ 55% (≥ 50% after completion of the anthracycline component of chemotherapy, if given)
- Adequate organ function

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPSACTregimens

EXCLUSIONS:

- Hypersensitivity to pertuzumab, trastuzumab, PACLitaxel, CARBOplatin* 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
- Pregnancy / Breastfeeding
- Baseline neutrophil count < $1.5x10^9$ cells/L
- Severe hepatic impairment

*If it is felt that the patient may have a major clinical benefit from CARBOplatin, it may in exceptional circumstances be feasible to rechallenge a patient with a prior mild hypersensitivity reaction e.g. using a desensitisation protocol, but only with immunology advice, premedication as advised, and a desensitisation protocol under carefully controlled conditions with resuscitation facilities available and medical and/or ITU/ HDU supervision

PRESCRIPTIVE AUTHORITY:

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

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Cardiac function (LVEF using ECHO or MUGA scan)
- Isotope GFR measurement (preferred) or GFR / Cr Clearance estimation

Regular tests:

- FBC, renal and liver profile before each cycle
- Cardiac function (MUGA or ECHO) every 12 weeks. Where there are signs of cardiac impairment four to eight weekly checks may be more appropriate.
- Assessment of peripheral neuropathy status as clinically indicated

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPSACTregimens

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 pertuzumab and trastuzumab after a dose delay or missed doses.
- Patients may continue therapy during periods of reversible chemotherapy-induced myelosuppression but they should be monitored carefully for complications of neutropenia during this time.

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.

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPSACTregimens

PACLitaxel and CARBOplatin:

Table 3: Dose Reduction Levels for PACLitaxel and CARBOplatin

	Starting Dose	Dose Level -1	Dose Level -2
PACLitaxel	80mg/m^2	70mg/m^2	60mg/m^2
CARBOplatin	AUC 6	AUC 5	AUC 4

Haematological:

Table 4: Dose modification of CARBOplatin and PACLitaxel in haematological toxicity

Day	ANC (x10^9/L)		Platelets (x10^9/L)	CARBOplatin Dose	PACLitaxel Dose
Day 1	≥ 1	and	≥ 75	100% Dose	100% Dose
	< 1	and/or	< 75	Delay treatment until recovery[a]	Delay treatment until recovery[a]
Day 8	< 0.5	and/or	< 50		Omit day 8 PACLitaxel dose
Day 1	Febrile Neutropenia			Decrease CARBOplatin dose by one dose level	
	< 0.5 for ≥ 7 days	or	< 10		
			10 to 50 with bleeding tendencies		
	Treatment delay for haematological toxicity > 1 week 1st occurrence			Decrease CARBOplatin dose by one dose level to AUC 5	
	2nd occurrence			Decrease CARBOplatin dose further for subsequent cycles to AUC 4	

[a]Treatment may be delayed for a maximum of 2 weeks.

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPSACTregimens

Renal and Hepatic Impairment:

Table 5: 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.			
PACLitaxel [b]	Renal impairment: no need for dose adjustment is expected. Haemodialysis: no need for dose adjustment is expected.	**Transaminases**		**Bilirubin**	**Dose of PACLitaxel**
		< 10 x ULN	and	≤ 1.25 x ULN	No dose reduction
		< 10 x ULN	and	1.26-2 x ULN	75% of original dose
		< 10 x ULN	and	2.01-5 x ULN	50% of original dose
		≥10 x ULN	and /or	>5 x ULN	Contraindicated
CARBOplatin [c]	**See note below***	No dose modification required			

[a] Phesgo® (renal and hepatic – SPC)
[b] PACLitaxel (renal and hepatic – Giraud et al (2023))
[c] CARBOplatin (renal and hepatic – NCCP Standardisation)

*Renal dysfunction and CARBOplatin:

- Patients with creatinine clearance values of <60 mL/minute are at greater risk of developing myelosuppression.
- If GFR between 20 to ≤ 30mL/minute, CARBOplatin should be administered with extreme caution
- If GFR ≤ 20mL/minute, CARBOplatin should not be administered at all If Cockcroft & Gault or Wright formula are used, the dose should be calculated as required per cycle based on a serum creatinine obtained within 48 hours of drug administration.

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPSACTregimens

- If isotope GFR is used, the dose can remain the same provided the serum creatinine is ≤ 110% of its value at the time of the isotope measurement. If the serum creatinine increases, consideration should be given to remeasuring the GFR or to estimating it using Cockcroft & Gault or Wright formulae.

Management of adverse events:

Table 6: Dose modification schedule based on adverse events

Adverse reactions	Recommended dose modification
Pertuzumab and Trastuzumab (Phesgo®)	
Reduction in LVEF to < 50% - associated with a fall of ≥ 10% points below pre-treatment values	Withhold treatment with pertuzumab/trastuzumab (Phesgo®) for at least 3 weeks. Pertuzumab/trastuzumab (Phesgo®) may be resumed if the LVEF has recovered to ≥ 50% or to a difference of < 10% points below pre-treatment values. No improvement or further decline, discuss with consultant and consider referral to cardiology.
Symptomatic heart failure	Discontinue
NCI-CTCAE Grade 4 hypersensitivity reactions	Discontinue
PACLitaxel	
Grade ≥ 2 motor or sensory neuropathy First Occurrence Persistent Grade ≥ 2 or 2nd occurrence	Decrease dose of PACLitaxel by 10mg/m^2. Decrease dose of PACLitaxel by a further 10mg/m^2
All other grade 2 non-haematological toxicity	Hold treatment until toxicity resolves to ≤ grade 1. Decrease subsequent doses by 10mg/m$^{2.}$
≥ Grade 3 reaction	Discontinue
Patients who cannot tolerate treatment after 2 dose reductions should be discussed with treating clinician regarding continuation of treatment.	

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPSACTregimens

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

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

Pertuzumab/trastuzumab (Phesgo®): Minimal **(Refer to local policy)**
PACLitaxel: Low **(Refer to local policy)**
CARBOplatin: High **(Refer to local policy)**

For information:

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:

Trastuzumab/pertuzumab (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.

PACLitaxel:

- All patients must be premedicated with corticosteroids, antihistamines, and H_2 antagonists prior to first dose of PACLitaxel treatment.
- The H_2 antagonist, famotidine, can potentially be omitted from the premedication requirements for PACLitaxel but the risk of hypersensitivity with this approach is unknown.
    - Caution is advised particularly for patients receiving PACLitaxel every 3 weeks. It is recommended that if famotidine is omitted that patients are monitored closely for any signs of hypersensitivity. Any hypersensitivity should be managed as per local policy.
    - Where a patient experiences hypersensitivity, consider the use of alternative H_2 antagonists **(Refer to local policy).**

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPSACTregimens

Table 7 outlines the suggested premedications prior to treatment with PACLitaxel.

Table 7: Suggested premedications prior to treatment with PACLitaxel

Day of treatment	Drug	Dose	Administration prior to PACLitaxel
Day 1	dexAMETHasone[a]	8mg IV	30 minutes
Day 1	Chlorphenamine	10mg IV	30 minutes
Day 1	Famotidine	20mg IV	30 minutes
Day 8[b] and thereafter	dexAMETHasone[a]	None	
Day 8 and thereafter	Chlorphenamine	10mg IV	30 minutes
Day 8 and thereafter	Famotidine[c]	20mg IV	30 minutes
[a]Dose of dexAMETHasone may be altered, in the event of hypersensitivity reaction, to 20 mg of dexAMETHasone orally 12 hour and 6 hour prior to re-challenge with PACLitaxel according to consultant guidance.			
[b]Dose of dexAMETHasone may be added from day 8 if increased risk or previous hypersensitivity reaction according to consultant guidance.			
[c]Dose of famotidine may be omitted in the absence of hypersensitivity reaction according to consultant guidance.			

OTHER SUPPORTIVE CARE:

- Myalgias and arthralgias may occur with PACLitaxel. Analgesic cover should be considered.
- G-CSF support may be required **(Refer to local policy)**

ADVERSE EFFECTS:

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

DRUG INTERACTIONS:

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

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPSACTregimens

REFERENCES:

1. van Ramshorst MS ET AL. Dutch Breast Cancer Research Group (BOOG). Neoadjuvant chemotherapy with or without anthracyclines in the presence of dual HER2 blockade for HER2-positive breast cancer (TRAIN-2): a multicentre, open-label, randomised, phase 3 trial. Lancet Oncol. 2018 Dec;19(12):1630-1640. doi: 10.1016/S1470-2045(18)30570-9. Epub 2018 Nov 6. PMID: 30413379.
2. van Ramshorst MS et al. Dutch Breast Cancer Research Group (BOOG). Toxicity of dual HER2-blockade with pertuzumab added to anthracycline versus non-anthracycline containing chemotherapy as neoadjuvant treatment in HER2-positive breast cancer: The TRAIN-2 study. Breast. 2016 Oct;29:153-9. doi: 10.1016/j.breast.2016.07.017. Epub 2016 Aug 5. PMID: 27498129.
3. van der Voort A, van Ramshorst MS, van Werkhoven ED, Mandjes IA, Kemper I, Vulink AJ, Oving IM, Honkoop AH, Tick LW, van de Wouw AJ, Mandigers CM, van Warmerdam LJ, Wesseling J, Vrancken Peeters MT, Linn SC, Sonke GS. Three-Year Follow-up of Neoadjuvant Chemotherapy With or Without Anthracyclines in the Presence of Dual ERBB2 Blockade in Patients With ERBB2-Positive Breast Cancer: A Secondary Analysis of the TRAIN-2 Randomized, Phase 3 Trial. JAMA Oncol. 2021 Jul 1;7(7):978-984. doi: 10.1001/jamaoncol.2021.1371. PMID: 34014249; PMCID: PMC8138752.
4. Appropriate chemotherapy dosing for obese adult patients with cancer: American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol 2012; 30 (13) 1553-1561.
5. Ekhart C, Rodenhuis S et al. CARBOplatin dosing in overweight and obese patients with normal renal function, does weight matter? Cancer Chemother Pharmacol 2009;64:115-122.
6. NCCN CARBOplatin dosing in adults. Available https://www.nccn.org/docs/default-source/clinical/order-templates/appendix_b.pdf?sfvrsn=6286822e_6
7. Wright JG, Boddy AV, et al, Estimation of glomerular filtration rate in cancer patients. British Journal of Cancer 2001; 84(4):452-459
8. Tan A, et al. Fixed-dose combination of pertuzumab and trastuzumab for subcutaneous injection plus chemotherapy in HER2-positive early breast cancer (FeDeriCa): a randomised, open-label, multicentre, non-inferiority, phase 3 study. Lancet Oncol. 2021 Jan; 22(1):85-97.
9. Giraud E L, Lijster B D, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. Available at: https://pubmed.ncbi.nlm.nih.gov/37269847/
10. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V5 2023. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPSACTregimens

11. Nissenblatt MJ. Karp GI. Bleeding risk with trastuzumab (Herceptin®) treatment JAMA 1999;282:2299-301.

12. Pertuzumab and Trastuzumab (Phesgo®) Summary of Product Characterisitics. Last updated: 02/03/2022. Accessed January 2024. Available at: https://www.ema.europa.eu/en/documents/product-information/phesgo-epar-product-information_en.pdf

13. PACLitaxel Summary of Product Characteristics. Last updated Sep 2022. Accessed January 2024. Available at: https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA2059-050-001_21092022103217.pdf

14. CARBOplatin Summary of Product Characteristics. Last updated: 22/03/2023. Accessed January 2024. Available at: https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA2059-032-001_22032023144546.pdf

Version	Date	Amendment	Approved By
1	20/12/2022		Prof Maccon Keane
2	10/08/2023	Updated exclusions and emetogenic potential	Prof Maccon Keane
3	10/07/2024	Regimen reviewed.Updated information regarding HER2 and LVEF in Eligibility section.Updated Regular Tests section.Removed Day 15 in Table 4.Aligned Table 5: aligned PACLitaxel (renal and hepatic) dose modifications to Giraud et al (2023).Updated Table 6. Adverse Effects and Drug Interactions sections removed and replaced with standard wording.	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPSACTregimens