Indication	The first line treatment of locally advanced or metastatic breast cancer in patients whose tumours significantly overexpress HER2 at the 3+ level or FISH positive and are **not suitable** for docetaxel. NB Any adjuvant HER2 therapy must have been completed more than 12 months prior to diagnosis of locally advanced or metastatic disease.
Treatment Intent	Palliative
Frequency and number of cycles	Repeat every 21 days Pertuzumab/trastuzumab SC and paclitaxel every 3 weeks for 6 cycles then continue pertuzumab / trastuzumab until progressive disease, unacceptable toxicity or patient choice. If disease progression is within the CNS alone, treatment with pertuzumab/trastuzumab can continue. NB patients can be switched between combination SC therapy (Phesgo®) or pertuzumab and trastuzumab IV therapy if the clinical need arises with the usual dosing interval.
Monitoring Parameters pre-treatment	• **Virology screening:** All new patients referred for systemic anti-cancer treatment should be screened for hepatitis B and C and the result reviewed prior to the start of treatment. Patients not previously tested who are starting a new line of treatment, should also be screened for hepatitis B and C. Further virology screening will be performed following individual risk assessment and clinician discretion. • **Cardiac monitoring:** • Cardiac function should be monitored at baseline (ECHO/MUGA and ECG), and every 12 weeks (ECHO or MUGA) during treatment or as clinically indicated. • Patients should have a pre-treatment left ventricular ejection fraction (LVEF) of >/= 50 %. • Record on cardiac monitoring record on KOMs. • **It is the prescribers' responsibility to check that the ECHO/MUGA result is satisfactory before continuing treatment.** • If signs of left ventricular dysfunction see SPC and algorithm for continuation and discontinuation of pertuzumab/trastuzumab SC based on LVEF assessments. • At each nurse assessment patients should be assessed for signs of dyspnoea. • Monitor FBC, U&E and LFT at each cycle and on day 8 and 15 of cycles 1 to 6. • FBC, U&Es and LFTs should be monitored every 3 months or as clinically indicated from cycle 7 onwards. • Day 1: If neuts >/=1.5 and PLT >/=100 continue, otherwise delay 1 week. • Day 8 and day 15: • If neuts 1.0-1.4 and PLT >/=100 and patient well continue with treatment. • If neuts <1.0 or PLT <100 defer 1 week. • **Hepatic impairment:** o **Paclitaxel:** If bilirubin < 1.25 x ULN and transaminase < 10 x ULN, dose at full dose. Otherwise consider dose reduction see table 1, not recommended in severe hepatic impairment. o There are no recommendations for dose reductions of pertuzumab and trastuzumab SC in hepatic impairment. • **Renal impairment:** o **Paclitaxel**: no dose reduction necessary. o Dose reductions of pertuzumab and trastuzumab SC are not required in mild to moderate renal impairment. There are no recommendations for dose reductions in severe renal impairment. • **Infusion-related/ injection reactions:** o **Paclitaxel:** Patients developing hypersensitivity reactions to Paclitaxel may be re-challenged with full dose Paclitaxel following prophylactic medication (e.g. famotidine 40mg po given 4 hours prior to treatment plus Hydrocortisone 100mg iv and chlorphenamine 10mg iv 30 minutes prior to treatment), then give paclitaxel over 3-6 hours (i.e. starting at over 6 hours and gradually increase rate if possible).

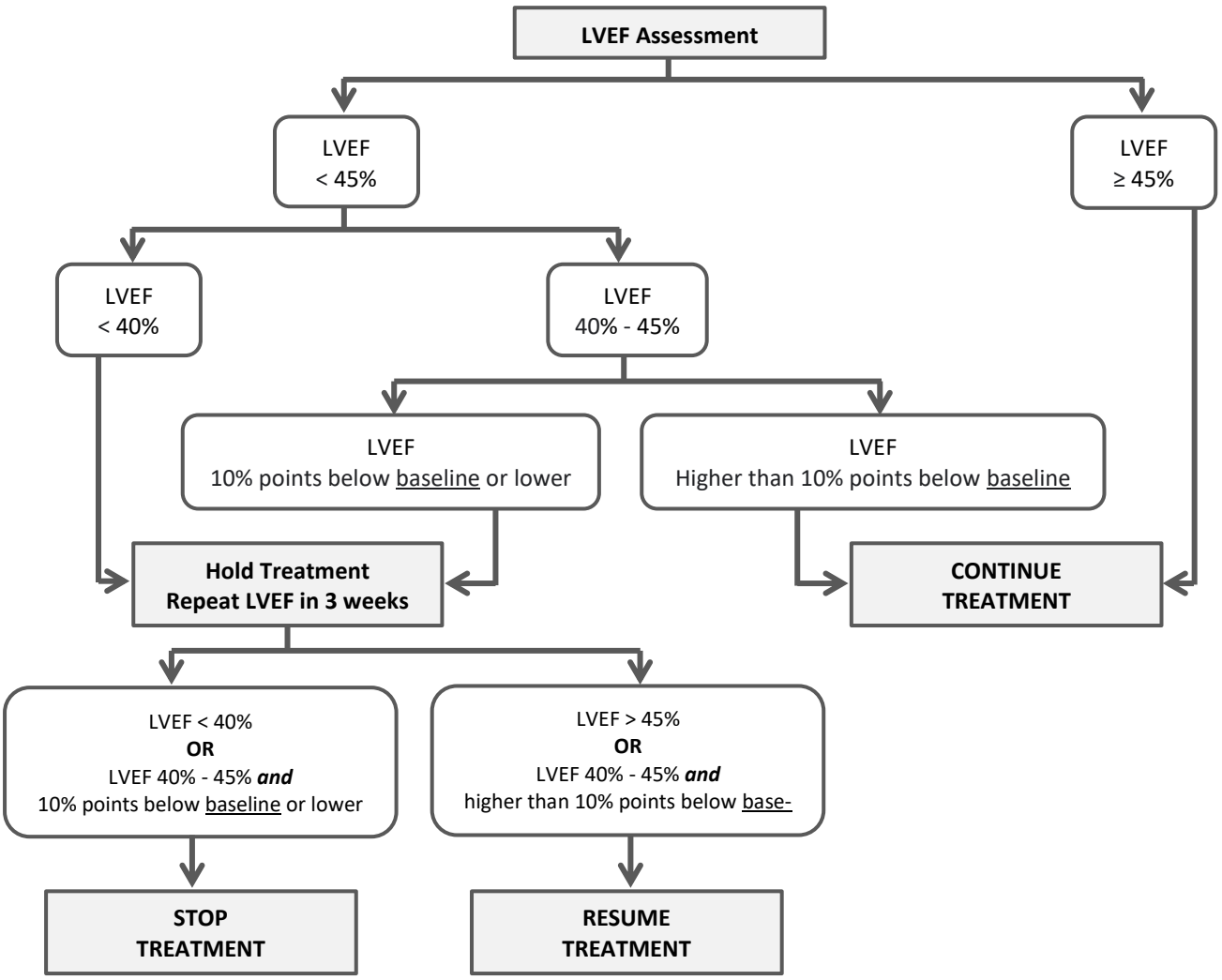
	○ If patients experience no hypersensitivity reactions after the first two doses of paclitaxel, remove pre-medication with dexamethasone, chlorphenamine and (if applicable) H2 antagonist from dose 3 onwards. ○ **Pertuzumab/trastuzumab SC: Injection duration and monitoring:** ○ The loading dose of pertuzumab/trastuzumab SC should be administered over 8 minutes, and the maintenance dose over 5 minutes. Patients must be observed closely for injection related adverse effects during administration and for 30 minutes after the completion of the loading dose of pertuzumab/trastuzumab SC and for 15 minutes after the completion of maintenance doses. If a significant injection-related reaction occurs, the injection should be slowed down or paused and appropriate medical therapies should be administered. Patients should be evaluated and carefully monitored until complete resolution of signs and symptoms. ○ Discontinue pertuzumab/ trastuzumab SC in the event of grade 4 hypersensitivity reaction. • **Administration of pertuzumab/trastuzumab SC** ○ Inject into the subcutaneous tissue of the thigh only. Injection sites should alternate between left and right thigh. New injections should be given at least 2.5 cm from the previous site. Do not inject at other sites of the body. ○ Pertuzumab/trastuzumab solution for subcutaneous injection should never be injected into areas where the skin is red, bruised, tender, or hard. ○ The dose should not be split between two syringes or between two sites of administration. ○ During treatment with pertuzumab/trastuzumab solution for subcutaneous injection, do not administer other medicinal products for subcutaneous use at the same site. ○ **Re-loading:** The loading doses of pertuzumab and trastuzumab SC should be repeated if the interval between injections is 6 weeks or more (i.e. if the doses are missed by 3 weeks or more), thereafter the maintenance dose can be given. NB This applies regardless of whether treatment was pertuzumab iv and trastuzumab iv or pertuzumab and trastuzumab SC. • **Dose Modification:** ○ Dose reduce Paclitaxel by 20% in the event of >/= grade 2 neuropathy and consider a delay until recovery to </= grade 1. ○ Consider omitting paclitaxel in event of recurrent >/= grade 3 neuropathy or recurrent OR persistent >/=grade 2 neuropathy following a dose reduction. ○ Dose reduction of paclitaxel should be considered if any other grade 3 or 4 non-haematological toxicity or repeat appearance of grade 2 (except N&V and alopecia). Delay until resolution of toxicity to </= grade 1. ○ No dose reductions are recommended for pertuzumab and trastuzumab SC. • **Common drug interactions (for comprehensive list refer to BNF/SPC):** ○ **Pertuzumab/trastuzumab SC:** No formal drug interaction studies have been performed. Caution with other cardiotoxic drugs. ○ **Paclitaxel:** Caution should be exercised when administering paclitaxel concomitantly with medicines known to inhibit either CYP2C8 or CYP3A4 (e.g. ketoconazole, erythromycin, fluoxetine, clopidogrel, cimetidine, ritonavir and nelfinavir); toxicity may be increased. CYP2C8 or CYP3A4 inducers (e.g. rifampicin, carbamazepine, phenytoin, efavirenz, nevirapine) may reduce efficacy. • **Missed dose:** • Pertuzumab/trastuzumab SC Re-loading: The loading doses of pertuzumab/trastuzumab SC should be repeated if the interval between injections is 6 weeks or more (i.e. if the doses are missed by 3 weeks or more), thereafter the maintenance dose can be given. NB This applies regardless of whether prior treatment was pertuzumab iv and trastuzumab iv or pertuzumab / trastuzumab SC. • **Driving and operating machinery:** Pertuzumab/trastuzumab SC may have a minor influence on the ability to drive and use machines. Patients experiencing injection-related reactions or dizziness should be advised not to drive and use machines until symptoms resolve.
References	CDF list V 1.333 accessed online 26.11.2024. BlueTeq form accessed online 26.11.2024. SPC accessed online 27.11.2024 KMCC protocol BRE-078 V1

NB For funding information, refer to CDF and NICE Drugs Funding List

Table 1 Dose modification for paclitaxel in hepatic impairment

Bilirubin	Transaminase	Percentage dose
</= 1.25 x ULN **AND**	<10 x ULN	100%
>1.25 to <2 x ULN		80 %
2-5 x ULN		50%
>5 xULN **OR**	>/= 10 x ULN	contraindicated

Algorithm for Continuation and Discontinuation of Pertuzumab and Trastuzumab based on LVEF assessment



Cycle 1 only 21 day cycle.

Day	Drug	Dose	Route	Infusion/ injection Duration	Administration
1	**Phesgo® (pertuzumab/ trastuzumab)**	**1200mg pertuzumab /600mg trastuzumab**	SC	Over 8 minutes	Inject 15 mL into the subcutaneous tissue of the left or right thigh over 8 minutes. Do not inject at other sites of the body. Injection sites should be rotated for successive injections.
	Patients should be observed for injection-related reactions and hypersensitivity reactions for 30 minutes following administration of Phesgo®, observation should be completed prior to any subsequent administration of chemotherapy.				
	Give pre-meds 30 minutes prior to paclitaxel				
	Dexamethasone	8mg	IV	bolus	
	Chlorphenamine	10mg	IV	bolus	Over 3 min through a fast running Sodium chloride 0.9% intravenous infusion
	Metoclopramide	20mg	IV	bolus	
	PACLITAXEL	**80mg/m²**	IV	Over 1 hour	Diluted in 250ml sodium chloride 0.9% (non-PVC bag and non PVC giving set) via in-line 0.22micron filter Flush with sodium chloride 0.9%
8	**Give pre-meds 30 minutes prior to paclitaxel**				
	Dexamethasone	8mg	IV	bolus	
	Chlorphenamine	10mg	IV	bolus	Over 3 min through a fast running Sodium chloride 0.9% intravenous infusion
	Metoclopramide	20mg	IV	bolus	
	PACLITAXEL	**80mg/m²**	IV	Over 1 hour	Diluted in 250ml sodium chloride 0.9% (non-PVC bag and non PVC giving set) via in-line 0.22micron filter. Flush with sodium chloride 0.9%
15	**Give pre-meds 30 minutes prior to paclitaxel**				
	Dexamethasone	8mg	IV	bolus	
	Chlorphenamine	10mg	IV	bolus	Over 3 min through a fast running Sodium chloride 0.9% intravenous infusion
	Metoclopramide	20mg	IV	bolus	
	PACLITAXEL	**80mg/m²**	IV	Over 1 hour	Diluted in 250ml sodium chloride 0.9% (non-PVC bag and non PVC giving set) via in-line 0.22micron filter. Flush with sodium chloride 0.9%
TTO	Drug	Dose	Route	Directions	
Day 1, 8 and 15	Metoclopramide	10mg	PO	3 times a day for 3 days after paclitaxel, then 10mg up to 3 times a day as required. (max. 30mg per day including 20mg pre-chemo dose) Do not take for more than 5 days continuously.	
	Dexamethasone	4mg	PO	OM for 2 days starting the day after paclitaxel dose. Take with or just after food, or a meal.	

Cycle 2 to 6: Repeat every 21 days

Day	Drug	Dose	Route	Infusion/ injection Duration	Administration
1	**Phesgo® (pertuzumab/ trastuzumab)**	**600mg pertuzumab /600mg trastuzumab**	SC	Over 5 minutes	Inject 10 mL into the subcutaneous tissue of the left or right thigh over 5 minutes. Do not inject at other sites of the body. Injection sites should be rotated for successive injections.
	Patients should be observed for injection-related reactions and hypersensitivity reactions for 15 minutes following administration of Phesgo®, observation should be completed prior to any subsequent administration of chemotherapy.				
	Give pre-meds 30 minutes prior to paclitaxel				
	Dexamethasone	8mg	IV	bolus	
	Chlorphenamine	10mg	IV	bolus	Over 3 min through a fast running Sodium chloride 0.9% intravenous infusion
	Metoclopramide	20mg	IV	bolus	
	PACLITAXEL	**80mg/m²**	IV	Over 1 hour	Diluted in 250ml sodium chloride 0.9% (non-PVC bag and non PVC giving set) via in-line 0.22micron filter Flush with sodium chloride 0.9%
8	**Give pre-meds 30 minutes prior to paclitaxel**				
	Dexamethasone	8mg	IV	bolus	
	Chlorphenamine	10mg	IV	bolus	Over 3 min through a fast running Sodium chloride 0.9% intravenous infusion
	Metoclopramide	20mg	IV	bolus	
	PACLITAXEL	**80mg/m²**	IV	Over 1 hour	Diluted in 250ml sodium chloride 0.9% (non-PVC bag and non PVC giving set) via in-line 0.22micron filter. Flush with sodium chloride 0.9%
15	**Give pre-meds 30 minutes prior to paclitaxel**				
	Dexamethasone	8mg	IV	bolus	
	Chlorphenamine	10mg	IV	bolus	Over 3 min through a fast running Sodium chloride 0.9% intravenous infusion
	Metoclopramide	20mg	IV	bolus	
	PACLITAXEL	**80mg/m²**	IV	Over 1 hour	Diluted in 250ml sodium chloride 0.9% (non-PVC bag and non PVC giving set) via in-line 0.22micron filter. Flush with sodium chloride 0.9%
TTO	Drug	Dose	Route	Directions	
Day 1, 8 and 15	Metoclopramide	10mg	PO	3 times a day for 3 days after paclitaxel, then 10mg up to 3 times a day as required. (max. 30mg per day including 20mg pre-chemo dose) Do not take for more than 5 days continuously.	
	Dexamethasone	4mg	PO	OM for 2 days starting the day after paclitaxel dose. Take with or just after food, or a meal.	

Cycles 7 onwards: repeat every 21 days

Day	Drug	Dose	Route	Injection Duration	Administration details
1	**Phesgo® (pertuzumab/ trastuzumab)**	**600mg pertuzumab/ 600mg trastuzumab**	SC	5 minutes	Inject 10 mL into the subcutaneous tissue of the left or right thigh over 5 minutes. Do not inject at other sites of the body. Injection sites should be rotated for successive injections.
	Patients should be observed for injection-related reactions and hypersensitivity reactions for 15 minutes following administration of Phesgo®				