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.
Treatment Intent	Palliative
Frequency and number of cycles	Pertuzumab, trastuzumab and docetaxel every 3 weeks for 6 cycles (or more at clinician discretion) then continue pertuzumab & trastuzumab until unacceptable toxicity or visceral progression.
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. • This regimen is restricted to patients whose tumours significantly overexpress HER2 at the 3+ level or FISH positive. • Monitor FBC, U&E and LFT at each cycle (cycles1-6). If neuts 1.0-1.4 and PLT >/=100 d/w consultant. If neuts >/= 1.5 and PLT >/= 100 continue with treatment. If neuts <1.0 or PLT <100 defer 1 week. (NB Pertuzumab and trastuzumab should not be reduced). • FBC, U&Es and LFTs should be monitored every 3 months or as clinically indicated from cycle 7 onwards. • **Renal and hepatic impairment:** o Docetaxel not recommended in severe hepatic impairment. A dose reduction of docetaxel may be made dependent on PS and liver function. o Dose reductions of pertuzumab are not required in mild to moderate renal impairment. There are no recommendations for dose reductions of pertuzumab in severe renal impairment or hepatic impairment. o There are no recommendations for dose adjustments of trastuzumab in renal or hepatic impairment. • At each nurse assessment patients should be assessed for signs of dyspnoea. • **Cardiac monitoring:** o Cardiac function should be monitored at baseline (ECHO/MUGA and ECG), at 3 months, at 6 months and then every 6 months (ECHO or MUGA) during treatment or as clinically indicated. o Record on cardiac monitoring record on KOMs. o **It is the prescribers' responsibility to check that the ECHO/MUGA result is satisfactory before continuing treatment.** I o **I**f signs of left ventricular dysfunction see SPC and algorithm for continuation and discontinuation of Pertuzumab and Trastuzumab based on LVEF assessment s. • **Re-loading:** The loading doses of trastuzumab (iv) and pertuzumab should be repeated if the interval between infusions is 6 weeks or more (i.e. if the doses are missed by 3 weeks or more), thereafter the maintenance dose can be given. • **Infusion duration and monitoring:** If the first trastuzumab (iv) dose was well tolerated (no infusion related reactions), then the second and subsequent doses may be administered over the shorter infusion time of 30 minutes. If pertuzumab was well tolerated on cycle 1 (no infusion related reactions), then the second and subsequent doses may be administered over the shorter infusion time of 30 minutes. If not then, continue to administer subsequent doses over 60 minutes. Observations should be taken every 30 minutes during the pertuzumab infusion and patients should be monitored for 1 hour after the infusion before starting trastuzumab. Patients must be observed closely for infusion related adverse effects for 6 hours after the start of the loading dose of trastuzumab (iv), 2 hours after the start of the second dose of trastuzumab (iv) and one hour after the start of subsequent doses.

	• Dose reduction of docetaxel should be considered if 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. Pertuzumab and trastuzumab should not be reduced. • If trastuzumab treatment is discontinued, pertuzumab should also be discontinued. • Ensure dexamethasone pre-medication (8mg bd for 3 days starting the day before docetaxel) is prescribed and given to the patient at new patient chat • **Severe allergic reactions to docetaxel** • If a patient commences 1st line treatment with docetaxel and has a severe allergic reaction to docetaxel and is then re-challenged unsuccessfully with docetaxel, they may receive paclitaxel, pertuzumab and intravenous trastuzumab. The dosing schedule of paclitaxel is 80mg/m^2 IV on days 1, 8 and 15 of a 21 day cycle. Patients should receive a total of 6 cycles or more of taxane based treatment. Paclitaxel (together with support medication) should be administered as per the KMCC BRE-036 protocol/regimen. • NB the following support medications are not required with paclitaxel: Co-codamol, filgrastim and oral dexamethasone pre-med (IV dexamethasone will be given).
References	KMCC protocol BRE-032 V8

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

Cycle 1

Day	Drug	Dose	Route	Infusion Duration	Administration
1	**PERTUZUMAB**	**840mg**	IV	60 min	In 250ml sodium chloride 0.9%
	Observations should be taken every 30 minutes during the pertuzumab infusion and patients should be monitored for 1 hour after the infusion before starting trastuzumab				
	TRASTUZUMAB	**Loading dose 8mg/kg**	IV	90 min	In 250ml sodium chloride 0.9%
	Patients must be observed closely for infusion related adverse effects for 6 hours after the start of trastuzumab				
2	Metoclopramide	20mg	IV		
	DOCETAXEL	**75mg/m²**	IV	1 hour	Sodium Chloride 0.9% 250ml
TTO	Drug	Dose	Route	Directions	
Day 1	Metoclopramide	10mg	PO	Up to 3 times a day for 3 days, then as required (max. 30mg per day including 20mg pre-chemo dose). Do not take for more than 5 days continuously.	
	Dexamethasone	8mg	PO	BD for 3 days, starting day before next cycle of docetaxel.	

Cycle 2-6

Day	Drug	Dose	Route	Infusion Duration	Administration
1	**PERTUZUMAB**	**420mg**	IV	See notes above	In 250ml sodium chloride 0.9%
	Observations should be taken every 30 minutes during the pertuzumab infusion and patients should be monitored for 1 hour after the infusion before starting trastuzumab				
	TRASTUZUMAB	**Maintenance dose 6mg/kg**	IV	See notes above	In 250ml sodium chloride 0.9%
	Start docetaxel after the end of the trastuzumab observation period (i.e. 2 hours after the start of the trastuzumab for cycle 2, then one hour from the start of the infusion for cycle 3 onwards).				
	Metoclopramide	20mg	IV		
	DOCETAXEL	**(75mg/m²)* (100mg/m²)***	IV	1 hour	Sodium Chloride 0.9% 250ml
	***The dose of docetaxel can be increased from 75mg/m² to 100mg/m² from cycle 2 onwards if patient is able to tolerate an increase in dose.**				
TTO	Drug	Dose	Route	Directions	
Day 1	Metoclopramide	10mg	PO	Up to 3 times a day for 3 days, then as required (max. 30mg per day including 20mg pre-chemo dose). Do not take for more than 5 days continuously.	
	Dexamethasone	8mg	PO	BD for 3 days, starting day before next cycle of docetaxel.	

Cycle 7 onwards.

Day	Drug	Dose	Route	Infusion Duration	Administration
1	**PERTUZUMAB**	**420mg**	IV	See notes above	In 250ml sodium chloride 0.9%
	Observations should be taken every 30 minutes during infusion and patients should be monitored for one hour after infusion before starting trastuzumab				
	TRASTUZUMAB	**6mg/kg**	IV	See notes above	In 250ml sodium chloride 0.9%
	Patients must be observed closely for infusion related adverse effects for one hour after the start of the infusion				

Algorithm for Continuation and Discontinuation of Pertuzumab and Trastuzumab based on LVEF assessments.