Indication	Neo-adjuvant treatment of BRCA+ or triple negative breast cancer
Treatment Intent	Neo-adjuvant
Frequency and number of cycles	EC every 21 days for 4 cycles followed by carboplatin & weekly paclitaxel every 21 days for 4 cycles.
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. • Consider using actual BSA. • **<u>Cycles 1-4 EC</u>** • ECG should be checked prior to cycle 1 and undertake ECHO/MUGA as clinically indicated. • Maximum cumulative dose of epirubicin = 950mg/m^2. • Monitor FBC, LFT and U&E at each cycle. • If neuts >/= 1 and PLT>/=100 continue with treatment. If neuts <1 or PLT <100 delay by 1 week. • Impaired renal and liver function – d/w consultant or registrar if bilirubin elevated. Epirubicin: if bilirubin is 24-51 µmol /L give 50% dose, if bilirubin is 52-85µmol/L give 25% dose, if bilirubin is >85µmol/L omit. • Dose reduction 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 • **<u>Cycles 5-8 Carboplatin & paclitaxel</u>** • EDTA/DTPA should be used to measure GFR prior to cycle 5. C+G may be used to estimate CrCl if there is a delay in obtaining EDTA result, CrCl must be>/=30ml/min. Repeat EDTA if creatinine clearance drops by 25%. • Monitor FBC, U&E and LFT prior to each cycle and on day 8 and 15. • If neuts <1 or PLT <100 delay D1 by 1 week or omit day 8/15. If neuts >/=1 and PLT>/=100 continue with treatment. • **Hepatic impairment:** • Carboplatin: No dose adjustment required. • Paclitaxel: If bilirubin < 1.25 x ULN and transaminase < 10 x ULN, dose at full dose. Otherwise consider dose reduction, not recommended in severe hepatic impairment. • **Renal impairment:** • Carboplatin: stop if CrCl<30ml/min • Paclitaxel: no dose reduction necessary. • **Management of adverse reactions and dose adjustments:** • 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, consider removing pre-medication with dexamethasone and chlorphenamine from dose 3 onwards • Patients developing hypersensitivity reactions to carboplatin: Mild/moderate reactions (grade 1-2) - If symptoms resolve after treatment with hydrocortisone and chlorphenamine, the infusion may be restarted at 50% rate for 30 mins, then, if no further reaction, increase to 100% rate. If symptoms do not resolve after treatment with hydrocortisone and chlorphenamine, do not restart the infusion. At consultant's discretion, patients may be re-challenged at a later date with additional prophylaxis. In the event of further reaction (grade 1-3), stop infusion and consider alternative treatment. Severe (grade 3): Do not restart infusion. Consider alternative treatment. Anaphylaxis (grade 4): Follow anaphylaxis protocol. Discontinue permanently and consider alternative treatment. • Dose reduce Paclitaxel by 20% in the event of >/= grade 2 neuropathy and consider delay until recovery to </= grade 1 • Stop paclitaxel in the event of recurrent >/= grade 3 neuropathy OR recurrent or persistent >/= grade 2 neuropathy following dose reduction • Dose reduction 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. • **Common drug interactions (for comprehensive list refer to BNF/SPC):** • Avoid concomitant use of paclitaxel with CYP2C8 or CYP3A4 inducers (e.g. rifampicin, carbamazepine, phenytoin) and inhibitors (e.g. ketoconazole erythromycin, fluoxetine, gemfibrozil, clopidogrel, cimetidine, ritonavir, nelfinavir). • Carboplatin: Caution with other nephrotoxic drugs. • Caution, ciclosporin increases concentration of epirubicin.
Reference(s)	BRE 059 V5 SPC accessed online 14.12.21 BNF accessed online 14.12.21 Changes made in line with 'SOP for removal of ranitidine on KMCC protocols and on aria regimens

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

Cycles 1-4 repeat every 21 days

Day	Drug	Dose	Route	Infusion Duration	Administration Details
Day 1	Dexamethasone	8mg	PO		
	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IVI	15 min	In 50ml Sodium chloride 0.9%
	EPIRUBICIN	**90mg/m^2**	as a slow IV bolus		Through the side of a fast running 0.9% sodium chloride intravenous infusion
	CYCLOPHOSPHAMIDE	**600mg/m^2**	as a slow IV bolus		Through the side of a fast running 0.9% sodium chloride intravenous infusion

Cycles 1-4 repeat every 21 days

TTO	Drug	Dose	Route	Directions
Day 1	Dexamethasone	6mg	PO	Every AM for 3 days Take with or after food, or meal
	Metoclopramide	10mg	PO	3 times a day for 3 days, then 10mg up to 3 times a day as required. Do not take for more than 5 days continuously.
	Ondansetron	8mg	PO	BD for 3 days
	Fligrastim	300 mcg or consider dose of 480 mcg if patient > 80kg	Sub cutaneous injection	Starting on day 3 for 5 days

Cycles 5-8 repeat every 21 days

Day	Drug	Dose	Route	Infusion Duration	Administration Details
Day 1	**Give pre-meds 30 minutes prior to paclitaxel**				
	Dexamethasone	8mg (may be reduced to 4mg on subsequent doses)	IV		Give 30 mins prior to paclitaxel through the side of a fast running sodium chloride 0.9% infusion.
	Chlorphenamine	10mg	IV	Slow Bolus	Give 30 mins prior to paclitaxel through the side of a fast running sodium chloride 0.9% infusion.
	Ondansetron	<75yrs 16mg >/=75yrs 8mg	IVI	15 min	In 50ml Sodium chloride 0.9%
	PACLITAXEL	**80mg/m^2** (NB dose of paclitaxel may be increased to 90mg/m^2 at clinician discretion)	IVI	1 hour	In 250ml Sodium Chloride 0.9% (non-PVC bag and non-PVC administration set) via in-line 0.22 micron filter.
	CARBOPLATIN	**AUC 6** Dose = AUC x (GFR + 25) **(max. 700mg)**	IVI	30 minutes	in 500ml 5% glucose
Days 8 & 15	Dexamethasone	8mg (may be reduced to 4mg on subsequent doses)	IV		Give 30 mins prior to paclitaxel through the side of a fast running sodium chloride 0.9% infusion.
	Chlorphenamine	10mg	IV	Bolus	Give 30 mins prior to paclitaxel through the side of a fast running sodium chloride 0.9% infusion.
	Metoclopramide	10mg	IV	Bolus	
	PACLITAXEL	**80mg/m^2** (NB dose of paclitaxel may be increased to 90mg/m^2 at clinician discretion)	IVI	1 hour	In 250ml Sodium Chloride 0.9% (non-PVC bag and non-PVC administration set) via in-line 0.22 micron filter.

Cycles 5-8 repeat every 21 days

TTO	Drug	Dose	Route	Directions
Day 1	Dexamethasone	6mg	PO	OM for 3 days Take with or after food, or meal
	Ondansetron	8mg	PO	BD for 3 days
	Filgrastim	300 mcg or consider dose of 480 mcg if patient > 80kg	SC	OD starting on day 3 for 5 days
Day 1, 8 & 15	Metoclopramide	10mg	PO	3 times a day for 3 days, then 10mg up to 3 times a day as required. Do not take for more than 5 days continuously.
Day 8 & 15	Dexamethasone	4mg	PO	OM for 2 days Take with or after food, or meal NB Dexamethasone iv included as part of pre-med before paclitaxel in cycles 5-8