PACLITAXEL CARBOPLATIN EC

INDICATION (ICD10) C50

1. BRCA positive or triple negative invasive adjuvant or neoadjuvant breast cancer. PS 0, 1 (weekly paclitaxel is unlicensed)

REGIMEN

Cycles 1 to 4 (Paclitaxel to be administered before carboplatin)

Day 1	Premedication 30 minutes prior to infusion	
	Dexamethasone	8mg IV bolus
	H_2 antagonist (for 1st 3 doses)	
	Chlorphenamine	10mg IV bolus
	PACLITAXEL	80mg/m^2 in 250ml* sodium chloride 0.9% IV infusion over 60 minutes
	CARBOPLATIN	AUC 5 (if CrCl used maximum 700mg) in 500ml glucose 5% IV infusion over 30 minutes
	Dose calculated by EDTA GFR or calculated (CrCl + 25) x AUC.	
Days 8 and 15	Premedication 30 minutes prior to infusion	
	Dexamethasone	8mg IV bolus
	H_2 antagonist (for 1st 3 doses)	
	Chlorphenamine	10mg IV bolus
	PACLITAXEL	80mg/m^2 in 250ml* sodium chloride 0.9% IV infusion over 60 minutes

Cycles 5 to 8

Day 1	EPIRUBICIN	90mg/m^2 IV bolus
	CYCLOPHOSPHAMIDE	500mg/m^2 IV bolus

* doses 162mg to 600mg in 500ml sodium chloride 0.9%

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 days
Paclitaxel weekly and carboplatin cycles 1 to 4
EC cycles 5 to 8 (may wish to change to EC dose dense instead)

ANTI-EMETICS

Moderate risk day 1 cycles 1 to 4
Low risk days 8 and 15 cycles 1 to 4
High risk day 1 cycles 5 to 8

CONCURRENT MEDICATION REQUIRED

Carboplatin	Anaphylaxis treatment should be prescribed if the patient has had an anaphylactic episode previously. Dexamethasone 20mg IV bolus Chlorphenamine 10mg IV bolus H_2 antagonist Carboplatin should be given at a slower rate e.g. 2-4 hours.
Paclitaxel	Ensure premedication given before paclitaxel
GCSF	7 days in EC arm, 3 days following each weekly paclitaxel.

EXTRAVASATION AND TYPE OF LINE / FILTERS

Carboplatin – possible irritant
Cyclophosphamide – neutral
Paclitaxel – vesicant
Epirubicin – vesicant

Administer Paclitaxel via polyethylene lined administration set with ≤0.22micron filter
Central line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs every dose
Paclitaxel carboplatin:
Neutrophils x 10^9/L ≥1.0 day 1 (if not delay), ≥0.8 on days 8 and 15 (if not omit clinician discretion)
Platelets x 10^9/L ≥100 day 1 (if not delay), ≥80 days 8 and 15 (if not omit clinician discretion)
EC:
Neutrophils x 10^9/L ≥1.0 day 1 (if not delay)
Platelets x 10^9/L ≥100 day 1 (if not delay)
ECHO required if patient has preexisting cardiac disease
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Carboplatin	Ototoxicity – monitor Neurotoxicity - monitor
Cyclophosphamide	may irritate bladder, drink copious volumes of water.
Epirubicin	Cardiotoxicity – monitor cardiac function. Epirubicin may be stopped in future cycles if signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue.
Paclitaxel	(2% risk of severe hypersensitivity) Reactions range from mild hypotension (light-headedness) to full cardiac collapse (anaphylactic shock). Discontinue infusion and resuscitate appropriate to reaction. If reaction is mild and settles promptly (i.e. within 5-10 minutes), cautiously restart at a slower rate under close supervision. If further reactions occur stop treatment.

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS
(not exhaustive list check SPC/BNF/Stockleys)

Cyclophosphamide	Cytochrome P450 enzyme inducers (e.g. rifampicin, carbamazepine, phenytoin, St Johns Wort, corticosteroids): may increase active cyclophosphamide metabolites. Allopurinol, Cimetidine and protease inhibitors: may increase active metabolites. Aprepitant, Ciprofloxacin, Fluconazole, Itraconazole: may reduce activation of cyclophosphamide and alter the effectiveness of treatment. Grapefruit juice: decreased or delayed activation of cyclophosphamide. Patients should be advised to avoid grapefruit juice for 48 hours before and on day of cyclophosphamide dose.
Paclitaxel	DOACs to be used with caution, need dose modifications or to be avoided eg apixaban Clopidogrel interacts with paclitaxel Paclitaxel is catalysed, by cytochrome P450 isoenzymes CYP2C8 and CYP3A4. inhibitors (e.g. erythromycin, fluoxetine, gemfibrozil) use with caution. inducors (e.g. rifampicin, carbamazepine, phenytoin, phenobarbital, efavirenz, nevirapine) use with caution.

DOSE MODIFICATIONS
Epirubicin maximum lifetime dose
= 650mg/m^2 (in patients with cardiac dysfunction or exposed to mediastinal irradiation)
= 1000mg/m^2 (with normal cardiac function)

Haematological
Previous neutropenic sepsis, Symptoms including diarrhoea, mucositis and leucopenia, discuss with Registrar or Consultant

Non-haematological
Paclitaxel
If patient complains of tinnitus, tingling of fingers and/or toes or motor weakness discuss with Consultant or Registrar before administration
If grade ≥2 neuropathy, consider paclitaxel dose reduction
If grade >3 peripheral neuropathy is >grade 3 omit further paclitaxel

Hepatic impairment
Epirubicin

Bilirubin 24-51micromol/L	give 50% dose
Bilirubin 52-85micromol/L or AST >4xULN	give 25% dose
Bilirubin >86micromol/L or Child Pugh C	not recommended

Paclitaxel
In the absence of Gilbert's syndrome:

Transaminase <10xULN and bilirubin ≤1.25xULN	no dose reduction
Transaminase <10xULN and bilirubin 1.26-2xULN	clinician discretion
Transaminase <10xULN and bilirubin 2·01-5xULN	clinician discretion
Transaminase ≥10xULN or bilirubin >5xULN	contraindicated

Renal impairment
Carboplatin

GFR/ calculated CrCl ≤20ml/min or ≤30ml/min with pre-existing severe renal impairment	contraindicated

Cyclophosphamide

CrCl 10-29ml/min	Consider giving 75% dose

REFERENCES