EC PACLITAXEL (dose dense)

INDICATION (ICD10) C50
1. Adjuvant or neoadjuvant high risk disease. PS 0, 1

REGIMEN
Cycles 1 to 4

Day 1	EPIRUBICIN	90mg/m^2 IV bolus
	CYCLOPHOSPHAMIDE	600mg/m^2 IV bolus

Cycles 5 to 8

Day 1	Premedication 30 minutes prior to infusion:	
	Dexamethasone	20mg IV bolus
	Chlorphenamine	10mg IV bolus
	PACLITAXEL	175mg/m^2 in 500ml* sodium chloride 0.9% IV infusion over 3 hours

* doses 84mg to 144mg in 250ml sodium chloride 0.9%

CYCLE FREQUENCY AND NUMBER OF CYCLES
EC every 14 days for 4 cycles
Paclitaxel every 14 days for 4 cycles

ANTI-EMETICS
High risk day 1 cycles 1 to 4 (consider aprepitant)
Low risk day 1 cycles 5 to 8

CONCURRENT MEDICATION REQUIRED

Paclitaxel	Ensure premedication given before paclitaxel
GCSF	GCSF for 7 days starting at least 24 hours after chemotherapy

EXTRAVASATION AND TYPE OF LINE / FILTERS
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 cycle
Neutrophils x 10^9/L ≥1.0 (0.8-1.0 on the day of chemo go ahead with GCSF support as per local policy).
Platelets x 10^9/L ≥100
Consider ECHO if patient has preexisting cardiac disease
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

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, potentially increasing the concentration of paclitaxel. Paclitaxel is catalysed, by cytochrome P450 isoenzymes CYP2C8 and CYP3A4. inhibitors (e.g. erythromycin, fluoxetine, gemfibrozil) use with caution. inducers (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 using paclitaxel 135mg/m^2
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	give 77% of original dose
Transaminase <10xULN and bilirubin 2·01-5xULN	give 51% of original dose
Transaminase ≥10xULN or bilirubin >5xULN	contraindicated

Renal impairment

Cyclophosphamide

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

REFERENCES

1. Del Maestro, L et al; Lancet 2015; 385: 1863 – 1872
2. Early Breast Cancer Trialists' Collaborative Group; Lancet 2019; published online Feb 7th: http://dx.doi.org/10.1016/S0140-6736(18)33137-4