

PACLITAXEL CARBOPLATIN

INDICATION (ICD10) C50

1. Recurrent metastatic breast cancer. PS 0, 1 or 2 (weekly paclitaxel is unlicensed)

REGIMEN

Drugs can be given in any order

Day 1 Premedication 30 minutes prior to infusion:

Dexamethasone 8mg IV bolus

Chlorphenamine 10mg IV bolus

PACLITAXEL 80mg/m² in 500ml* 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.

Day 8 PACLITAXEL 80mg/m² in 500ml* sodium chloride 0.9% IV infusion over 60 minutes

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

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 days up to 6 cycles

ANTI-EMETICS

Moderate risk day 1

Low risk day 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

EXTRAVASATION AND TYPE OF LINE / FILTERS

Carboplatin - irritant

Paclitaxel – vesicant

Administer paclitaxel via polyethylene lined administration set with ≤0.22micron filter

Central or peripheral line

INVESTIGATIONS

Blood results required before SACT administration

FBC, U&E and LFTs, creatinine days 1 and 8

Neutrophils x 10⁹/L ≥1.5

Platelets x 10⁹/L ≥100

GFR assessed using EDTA result or calculated creatinine clearance at the Consultant's discretion.

Baseline weight and every cycle

MAIN TOXICITIES AND ADVERSE REACTIONS

Carboplatin	Ototoxicity – monitor Neurotoxicity - monitor
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)

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.
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DOSE MODIFICATIONS

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 giving 75% dose

If grade > 3 peripheral neuropathy is $> \text{grade } 3$ omit further paclitaxel

Hepatic impairment

Paclitaxel

In the absence of Gilbert's syndrome:

Transaminase $< 10 \times \text{ULN}$ and bilirubin $\leq 1.25 \times \text{ULN}$	no dose reduction
Transaminase $< 10 \times \text{ULN}$ and bilirubin 1.26-2xULN	clinician discretion
Transaminase $< 10 \times \text{ULN}$ and bilirubin 2.01-5xULN	clinician discretion
Transaminase $\geq 10 \times \text{ULN}$ or bilirubin $> 5 \times \text{ULN}$	contraindicated

Renal impairment

Carboplatin

GFR/ calculated CrCl $\leq 20 \text{ml/min}$ or $\leq 30 \text{ml/min}$ with pre-existing severe renal impairment	contraindicated
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REFERENCES