PACLITAXEL CISPLATIN

INDICATION (ICD10) C56

1. First line treatment of ovarian cancer for carboplatin allergic patients.
2. Recurrent ovarian cancer for carboplatin allergic patients.
   PS 0, 1 or 2

REGIMEN

Drugs can be given in any order

Day 1 Premedication 30 minutes prior to infusion:

Dexamethasone	20 mg IV bolus
H_2 antagonist	
Chlorphenamine	10 mg IV bolus
PACLITAXEL	175mg/m^2 in 500ml* sodium chloride 0.9% IV infusion over 3 hours
Prehydration	
CISPLATIN	60mg/m^2 in 1000ml sodium chloride 0.9% IV infusion over 2 hours
Posthydration	

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

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 days for 6 cycles

ANTI-EMETICS

High emetic risk day 1

CONCURRENT MEDICATION REQUIRED

Cisplatin	Ensure adequate pre and post hydration. If urine output is <100 ml/hour or if patient gains >2kg in weight during IV administration post cisplatin give 20-40mg furosemide PO/IV.
Paclitaxel	Ensure premedication given before paclitaxel

EXTRAVASATION AND TYPE OF LINE / FILTERS

Cisplatin - exfoliant
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 every cycle
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
GFR assessed using EDTA result or calculated creatinine clearance at the Consultant's discretion.
CA125 baseline and day 1 every cycle
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Cisplatin	Nephrotoxicity – ensure adequate pre and post hydration is prescribed. Ototoxicity – assess patient for tinnitus or hearing abnormalities.
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)

Cisplatin	Aminoglycosides increased risk of nephrotoxicity and ototoxicity. Renal function should be well monitored and audiometric tests as required. Carboplatin can cause a decrease in phenytoin serum levels. This may lead to reappearance of seizures and may require an increase of phenytoin dosages.
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

Non-haematological

If patient complains of tinnitus, tingling of fingers and/or toes or motor weakness discuss with Consultant or Registrar before administration

Hepatic impairment

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

Cisplatin

GFR >60ml/min	give 100% dose
GFR 45-60ml/min	give 75% dose
GFR <45ml/min	not recommended

REFERENCES