PACLITAXEL weekly CARBOPLATIN weekly

INDICATION (ICD10) C56

1. Recurrent ovarian cancer previously treated.
2. Advanced cervical, vaginal and vulval, endometrial 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	20 mg IV bolus
	H_2 antagonist	
	Chlorphenamine	10 mg IV bolus
	PACLITAXEL	80mg/m^2 in 500ml* sodium chloride 0.9% IV infusion over 60 minutes
	CARBOPLATIN	AUC 2 in 500ml glucose 5% IV infusion over 30 minutes
		Dose calculated by EDTA GFR or calculated (CrCl + 25) x AUC.
Day 8	Premedication 30 minutes prior to infusion:	
	Dexamethasone	20 mg IV bolus
	H_2 antagonist	
	Chlorphenamine	10 mg IV bolus
	PACLITAXEL	80mg/m^2 in 500ml* sodium chloride 0.9% IV infusion over 60 minutes
	CARBOPLATIN	AUC 2 in 500ml glucose 5% IV infusion over 30 minutes
		Dose calculated by EDTA GFR or calculated (CrCl + 25) x AUC.
Day 15	Premedication 30 minutes prior to infusion:	
	Dexamethasone	20 mg IV bolus
	H_2 antagonist	
	Chlorphenamine	10 mg IV bolus
	PACLITAXEL	80mg/m^2 in 500ml* sodium chloride 0.9% IV infusion over 60 minutes
	CARBOPLATIN	AUC 2 in 500ml glucose 5% IV infusion over 30 minutes
		Dose calculated by EDTA GFR or calculated (CrCl + 25) x AUC.

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

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 28 days for 2 to 4 cycles
Patients may be switched to paclitaxel carboplatin 21 day regimen according to response.

ANTI-EMETICS

Moderate risk days 1, 8 and 15

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 IV bolus 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 10^9/L ≥1.5 (omit days 8 and 15 rather than delay)
Platelets x 10^9/L ≥100 (omit days 8 and 15 rather than delay)
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

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.

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 paclitaxel dose reduction
If grade >3 peripheral neuropathy is >grade 3 omit further paclitaxel

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

Carboplatin

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

REFERENCES

1. Rose et al, Gynaecological Oncology 2005, 96, page 296-300.
2. Leiser et al International Journal of Gynaecological Cancer 2007, 17, page 379-86.