

PACLITAXEL weekly CARBOPLATIN

INDICATION (ICD10) C56

1. Consider for advanced serous ovarian 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 paclitaxel: Chlorphenamine 10mg IV bolus Dexamethasone 8mg IV bolus			
	PACLITAXEL	80mg/m ²	IV infusion	#ml sodium chloride 0.9% over 60 minutes
	CARBOPLATIN	AUC* 5	IV infusion	#ml glucose 5% over 30 minutes
Day 8	Premedication 30 minutes prior to paclitaxel: Chlorphenamine 10mg IV bolus Dexamethasone 8mg IV bolus			
	PACLITAXEL	80mg/m ²	IV infusion	#ml sodium chloride 0.9% 60 minutes
	Day 15	Premedication 30 minutes prior to paclitaxel: Chlorphenamine 10mg IV bolus Dexamethasone 8mg IV bolus		
PACLITAXEL		80mg/m ²	IV infusion	#ml sodium chloride 0.9% over 60 minutes

*Dose calculated by EDTA GFR or calculated (CrCl + 25) x AUC.

If CrCl used maximum 700mg

Elderly, poor PS, heavily pretreated patients should be started on 60mg/m² paclitaxel.

diluent volume for dose prescribed as per national standardised product specification

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 days up to 6 cycles

If required, can be reduced to 28 day cycle, giving patients a week off paclitaxel at the clinician's discretion.

ANTI-EMETICS

Moderate risk day 1

Low risk days 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 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 or DEHP free administration set with ≤ 0.22 micron filter
Central or peripheral line

INVESTIGATIONS

Blood results required before SACT administration

U&E including Mg ⁺⁺ (>0.4) and LFTs	baseline and every week (not required on days 8 and 15 if normal day 1)
FBC (or POCHI), U&E including Mg ⁺⁺ (>0.4) and LFTs Neutrophils x 10 ⁹ /L ≥ 1.0 provided patient is well day 1, ≥ 1.0 days 8 & 15 (delay day 1 but omit days 8 & 15) Platelets $\geq 100 \times 10^9$ /L day 1, ≥ 75 days 8 & 15 (delay day 1 but omit days 8 & 15)	baseline and every week
GFR assessed using EDTA result (BMI <19 or >30 or calculated creatinine clearance at the Consultant's discretion)	baseline and every cycle
Serum creatinine	baseline and every cycle
CA125	baseline and day 1 every cycle
Virology	before cycle 1 if not previously checked
Weight	baseline 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 paclitaxel dose reduction

If grade > 3 peripheral neuropathy is $>$ grade 3 omit further paclitaxel

Hepatic impairment

Carboplatin

No need for dose adjustment is expected

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 $1.26 - 2 \times \text{ULN}$	give 77% of original dose
Transaminase $< 10 \times \text{ULN}$ and bilirubin $2.01 - 5 \times \text{ULN}$	give 51% of original dose
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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Paclitaxel

No need for dose adjustment is expected

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.

Assessments

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing
Clinical assessment	X		Pre cycle		Pre cycle	Every cycle
SACT assessment (PS and toxicities)	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	Every dose
U&E, calcium, magnesium & LFT	X	X	X	X	X	Every dose (see above)
CrCl	X	X	X	X	X	Every cycle
CT scan	X					At cycle 6, Inform consultant team if not booked
Informed consent	X					Verbal each cycle
Height	X					
Weight recorded	X	X	X	X	X	Every cycle