PACLITAXEL CARBOPLATIN

INDICATION (ICD10) C15, C54, C56, C67, D37, D39, D41,

1. Oesophago-gastric cancer with contraindication to fluoropyramidines (unlicensed).
2. Second line incurable locally advanced or metastatic urothelial bladder cancer, when cisplatin-based chemotherapy is unsuitable.
3. First line treatment of ovarian cancer.
4. Recurrent ovarian cancer.
5. Adjuvant endometrial cancer
6. Advanced endometrial cancer.
7. Advanced, metastatic and recurrent cervical carcinoma.
8. Advanced vulval and vaginal cancer
9. Unknown primary if appropriate
   PS 0, 1 or 2

REGIMEN

Drugs can be given in any order

Day 1	**Premedication** 30 minutes prior to paclitaxel: Chlorphenamine 10mg IV bolus Dexamethasone 20mg IV bolus			
	PACLITAXEL	175mg/m^2	IV infusion	#ml sodium chloride 0.9% over 3 hours
	CARBOPLATIN	AUC* 5	IV infusion	#ml glucose 5% over 30 minutes

*Dose calculated by EDTA GFR or calculated (CrCl + 25) x AUC.
Non-gynae indications - maximum dose when using CrCl (125+25 x AUC)mg
Gynae cancer - maximum dose when using CrCl is 700mg

diluent volume for dose prescribed as per national standardised product specification

CYCLE FREQUENCY AND NUMBER OF CYCLES

Oesophageal - every 21 days up to 6 cycles (may be given for 8 cycles in certain circumstances)
Bladder - every 21 days up to 8 cycles
Cervix – every 21 days for 6 cycles
Endometrium adjuvant – every 21 days for 4 cycles
Endometrium advanced – every 21 days for 6 cycles
Ovarian first line - every 21 days for up to 6 - 8 cycles
Ovarian advanced - every 21 days for 6 cycles
Vulval and vaginal – every 21 days for 6 cycles

ANTI-EMETICS

Moderate risk day 1

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 ≤0.22micron filter
Central or peripheral line

INVESTIGATIONS

Blood results required before SACT administration

FBC, U&E including Mg^{++} (>0.4) and LFTs Neutrophils x 10^9/L ≥1.5 (oesophago-gastric) Neutrophils x 10^9/L≥1.0 (urothelial and gynae) Platelets ≥100x10^9/L	baseline and every cycle
GFR assessed using EDTA result (gynae patients 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 ovarian, or as required endometrial patients
Virology	before cycle 1 if not previously checked
Weight	baseline 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 giving 75% paclitaxel dose

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 <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

Paclitaxel

No need for dose adjustment is expected

REFERENCES

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 cycle
U&E, calcium, magnesium & LFT	X	X	X	X	X	Every cycle
CrCl	X	X	X	X	X	Every cycle
CA125	X	X	X	X	X	Every cycle ovarian, as required endometrial
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