PACLITAXEL & CARBOPLATIN

1. First-line treatment of advanced ovarian or endometrial cancer.
2. A treatment option for women whose ovarian cancer responded to first-line platinum-based therapy, but relapsed more than 6 months after completion of first-line treatment. NICE approved May 2005
3. An option for treatment of advanced cervical cancer

Drugs/Dosage:	Paclitaxel	175mg/m^2	IV	Day 1
	Carboplatin	AUC 5*	IV	Day 1 (see Comments)

*Carboplatin dose of AUC 6 should be considered if Cockcroft and Gault predicts GFR > 60ml/min and fit patient. Adjust to AUC 5 once EDTA available.

Administration: Paclitaxel in 500ml 0.9% sodium chloride over 3 hours via non–PVC administration set with a 0.2 micron in-line filter
Followed by: Carboplatin diluted in 250ml 5% glucose over 30 – 60 minutes

Frequency: 3 weekly cycle

Ovary/endometrial:	6 cycles of both paclitaxel and carboplatin; paclitaxel only to be extended to a maximum of 8 cycles if clinical benefit shown
Cervix:	May be treated beyond 6 cycles, until toxicity or disease progression (in 1st line setting in combination with bevacizumab, if funding approved)

Main Toxicities: infusion-related hypersensitivity reactions; myelosuppression; myalgia / arthralgia; alopecia; peripheral neuropathy

Anti-emetics: highly emetogenic

Extravasation: paclitaxel is a vesicant

Regular investigations:	FBC	Day 1
	LFTs & U&Es	Day 1
	CA 125	Day 1
	EDTA	prior to Cycle 1 (if available – see Comments)

Comments: Pre-medication:

Dexamethasone	16mg	IV 60 mins prior to paclitaxel administration
Chlorphenamine	10mg	IV 30–60 mins prior to paclitaxel administration
Ranitidine	50mg	IV 30–60 mins prior to paclitaxel administration

Carboplatin dose should be calculated using the Calvert Formula:
Dose = Target AUC x (25 + GFR)

Cycle 1 may be given using the Cockcroft and Gault formula to predict creatinine clearance if the EDTA is not yet available. When using C&G, a “cap” of 125 ml/min should be used for carboplatin dose calculations.

Carboplatin dose should be re-calculated using the EDTA result for subsequent cycles (do not “cap”). EDTA should only be repeated if there is a 30% change in serum creatinine.

Reason for Update: cervical indication updated	Approved by Consultant: Dr A Stewart
Version: 8	Approved by Lead Chemotherapy Nurse: P Deery
Supersedes: Version 7	Date: 2.10.14
Prepared by: S Taylor	Checked by: C Tucker

For patients who experience a hypersensitivity reaction to carboplatin, see the SWSH Carboplatin Hypersensitivity Guidelines.

Dose Modifications

Haematological Toxicity:	Neutrophils < 1.5** x 10^9/l or Platelets < 100 x 10^9/l	Delay for 1 week. Repeat FBC and, if within normal parameters, resume treatment.

** If being given in the adjuvant setting and neutrophils 1.0 – 1.4 x 10^9/l, proceed with treatment, with G-CSF prophylaxis, without any delay. If in doubt, discuss with Consultant.

If neutrophils < 0.5 x 10^9/l for > 7 days, or febrile neutropenia, or platelets < 50 x 10^9/l: consider reducing the dose of both drugs in further cycles to paclitaxel 135mg/m2 and carboplatin AUC 4.

Renal Impairment: Carboplatin is contra-indicated if CrCl < 20 ml/min.

Hepatic Impairment: For paclitaxel, if bilirubin < 1.25 x ULN and ALT < 10 x ULN, proceed with full dose. Otherwise, consider a dose reduction. Not recommended in severe hepatic impairment.

Neuropathy: If a Grade 2 or worse peripheral neuropathy develops, paclitaxel should be reduced to 135mg/m^2 in all subsequent cycles.
If progressive neuropathy is observed after this dose reduction, then treatment with paclitaxel should be discontinued.

Myalgia / Arthralgia: Due to paclitaxel and often co-exist, usually Grade 1 or 2. Management consists of prescribing NSAIDs and reassuring patient that it is self-limiting.

Reference: ICON 3 Trial, Medical Research Council, April 1995
Tinker, AV et al; Gynecol Oncol 2005; 98 (1): 54 – 58 (cervical use)
Sit, AS et al; Cancer Invest 2004; 22 (3): 368 – 373 (cervical use)