GEMCITABINE AND CARBOPLATIN

A treatment option for platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer at second or subsequent recurrence *(i.e. for 3rd or subsequent line use)*

NICE do not approve the use of this regimen at the first recurrence of platinum-sensitive disease (TA 389)

Drug / Dosage:	Gemcitabine 1000mg/m^2	IV	Day 1 and Day 8
	Carboplatin AUC 4	IV	Day 1

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.

Administration: Gemcitabine diluted in 250 ml 0.9% sodium chloride and infused over 30 minutes
then
Carboplatin diluted in 250 ml 5% glucose and infused over 30 - 60 minutes

Frequency: 3 weekly cycle for 6 cycles

Main Toxicities: myelosuppression; erythematous rash; flu-like syndrome; peripheral oedema (mild-moderate & reversible)

Anti- emetics: Day 1: highly emetogenic; Day 8: mildly emetogenic

Extravasation: non-vesicants

Regular Investigations:	FBC	Day 1 and Day 8
	U&Es	Day 1
	LFTs	Day 1
	CA 125	Day 1
	EDTA	prior to Cycle 1 (if available – see Comments)

Comments:

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

If the decision is made to substitute carboplatin with cisplatin, then the locally agreed dose is **cisplatin 70mg/m^2** IV on Day 1 of each cycle. This should be administered with pre- and post-hydration according to standard locally agreed practice, plus fluid balance / urine monitoring.

Reason for Update: indication updated in line with NICE 2016 guidance	Approved by Consultant: Dr A Michael
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Dose Modifications

Haematological Toxicity:

Day 1:

Neutrophils < 1.5 x 10^9/l
or
Platelets < 100 x 10^9/l

Delay treatment for 1 week. Repeat FBC and, if normal, proceed with treatment*.

*Reduce the gemcitabine dose to 75% of the original cycle initiation dose if any of the following have occurred:

- Neutrophils < 0.5 x 10^9/l for > 5 days
- Neutrophils < 0.1 x 10^9/l for > 3 days
- Febrile neutropenia
- Platelets < 25 x 10^9/l
- Cycle delay of more than one week due to toxicity

Day 8:

Neutrophils		Platelets	Gemcitabine
> 1.5 x 10^9/l	and	≥ 100 x 10^9/l	Give full dose
1.0 – 1.5 x 10^9/l	or	75 – 100 x 10^9/l	Give 50% dose
< 1.0 x 10^9/l	or	< 75 x 10^9/l	Omit **(do not defer)**

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

If CrCl < 30ml/min, consider gemcitabine dose reduction – clinical decision

GFR (ml/min)	Cisplatin Dose
≥ 60	Give 100%
45 – 59	Give 75%
< 45	Withhold cisplatin

Hepatic Impairment: If bilirubin > 27 µmol/L, initiate treatment with gemcitabine 800mg/m^2

References:

Pfisterer et al; JCO 2006; 24: 4699 – 4707
No reference for cisplatin dose, but agreed local practice