PEMETREXED AND CARBOPLATIN

1. An option for first-line treatment of locally advanced or metastatic NSCLC if tumour histology is large-cell or adenocarcinoma, and who are considered unsuitable for cisplatin
2. For patients with unresectable malignant pleural mesothelioma and performance status 0 or 1 who are considered unsuitable for cisplatin
3. Re-challenge in mesothelioma if PFS > 12 months after 1st line pemetrexed & platinum

Drugs/Dosage:	Pemetrexed	500mg/m^2	IV	Day 1
	Carboplatin	AUC 5 (see Comments)	IV	Day 1

Other drugs: **Folic acid** 400µg po od starting at least 5 days before first treatment and continuing until 3 weeks after the last pemetrexed dose
Vitamin B_{12} 1000µg by im injection, starting any day in the 7 days before first treatment and then given once every 9 weeks (can be given on same day as pemetrexed) until 3 weeks after last pemetrexed dose

Pre-medication: (to reduce incidence/severity of skin reactions as well as anti-emetic role)
Dexamethasone 4mg po bd for 5 days, commencing the morning of the day prior to chemotherapy

Administration: Pemetrexed in 100ml sodium chloride 0.9% and infused over 10 minutes
then, 30 minutes after end of pemetrexed administration:
Carboplatin in 250ml 5% glucose over 30 minutes

Frequency: 3 weekly cycle
Mesothelioma: up to 6 cycles, dependent on subjective and objective response
NSCLC: 4 cycles in palliative context is usually adequate, but for patients with impressive objective response and excellent tolerability, consideration should be given to consolidating to a maximum of 6 cycles (especially as now no access to maintenance pemetrexed for these patients)

Main Toxicities: myelosuppression; mucositis; skin rash; alopecia (mild); diarrhoea; renal toxicity; ovarian failure/infertility

Anti-emetics: highly emetogenic (Note: further dexamethasone **not** required as well as that supplied as pre-medication above)

Extravasation: non vesicants

Regular Investigations:	FBC	Day 1	
	U&Es	Day 1	
	LFTs	Day 1	
	EDTA	prior to 1st cycle	
	CT scan	Mesothelioma:	prior to 1st cycle and after Cycle 3
		NSCLC:	prior to 1st cycle and after Cycle 2

Reason for Update: info about other brands apart from Alimta removed; pemetrexed in N/S; need for in-line filter removed	Approved by Consultant: Dr A Mehta
Version: 8	Approved by Lead Chemotherapy Nurse: S Wills-Percy
Supersedes: Version 7	Date: 7.9.17
Prepared by: S Taylor	Checked by: C Tucker

Comments: 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.

Non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided from 5 days before each dose of pemetrexed until 2 days after each dose.

Dose Modifications

Haematological Toxicity:

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

Delay 1 week. Repeat FBC - if within normal parameters, proceed with 100% doses.

If there are 2 or more delays, a 25% dose reduction of both carboplatin and pemetrexed may be considered. If in doubt, discuss with Consultant.

Renal Impairment:

CrCl (ml/min)	Pemetrexed Dose
≥ 45	Give 100% dose
< 45	Not recommended

If EDTA or calculated CrCl < 20ml/min, carboplatin is contra-indicated.

Hepatic Impairment: No dose adjustments indicated. Pemetrexed is primarily renally excreted unchanged. However, it has not been studied in patients with hepatic impairment.

Other Toxicities:

	Dose of Pemetrexed	Dose of Carboplatin
Grade 3 or 4 mucositis	Give 50% **of previous dose**	Give 100% **of previous dose**
Any other Grade 3 or 4 toxicities, or any diarrhoea requiring hospitalisation	Give 75% of previous dose	Give 75% of previous dose

If a patient suffers **any Grade 3 or 4 toxicity** after 2 dose reductions, **treatment must be reviewed by Consultant.**

References: Vogelzang, N et al; JCO (2003); 21 (14): 2636 – 2644 (mesothelioma)
Hughes, A et al; JCO (2002); 20 (16): 3533 – 3544 (mesothelioma)
Scagliotti, GV et al; JCO 2008; 26 (21): 3543 – 3551 (NSCLC)