PEMETREXED AND CISPLATIN

1. An option for first-line treatment of locally advanced or metastatic NSCLC if tumour histology is large-cell or adenocarcinoma (NICE 2009)
2. Second-line treatment of locally advanced or metastatic NSCLC, in patients with EGFR-TK mutation and which has progressed on first-line EGFR inhibitor
3. For patients with unresectable malignant pleural mesothelioma and performance status 0 or 1 (NICE 2008)
4. Re-challenge in mesothelioma if PFS > 12 months after 1st line pemetrexed & platinum

Drugs/Dosage:	Pemetrexed	500mg/m^2	IV	Day 1
	Cisplatin	75mg/m^2	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: 1 litre 0.9% sodium chloride + 20mmol KCl + 10mmol $MgSO_4$ IV over 2 hours
Pemetrexed in 100ml sodium chloride 0.9% over 10 minutes
then; Mannitol 20% 100ml IV over 15 minutes
then; **Cisplatin** in 1 litre 0.9% sodium chloride IV over 3 hours
1 litre 0.9% sodium chloride + 20mmol KCl + 10mmol $MgS0_4$ IV over 2 hours
500ml sodium chloride 0.9% IV **or** 500mls – 1 litre water orally over 1 hour

Frequency:	Mesothelioma:	3 weekly for up to 6 cycles, dependent on response
	NSCLC:	4 cycles in palliative context is usually adequate, but for patients with impressive objective response and excellent tolerability, consideration may be given to consolidating to a maximum of 6 cycles

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

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

Extravasation: non vesicants

Regular Investigations:	FBC	Day 1	
	LFTs and U&Es	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

Comments: Cycle 1 may be given using the Cockcroft and Gault formula to predict creatinine clearance if the EDTA is not yet available. Cisplatin dose should be re-calculated using the EDTA result for subsequent cycles. EDTA should only be repeated if there is a 30% change in serum creatinine.

Reason for Update: info about brands other than 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

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

Check electrolytes – additional supplements of magnesium, potassium or calcium may be required.

Weight should be recorded prior to and at the end of cisplatin treatment, and a strict fluid balance chart should be maintained. An average urine output of at least 100ml/hr must be maintained throughout treatment, and cisplatin infusion should not be commenced unless this urine output is achieved. If the urine output is inadequate, the patient should be assessed and urine output increased by administering 500ml sodium chloride 0.9% IV +/- furosemide 20 – 40mg. Furosemide 20 – 40mg po may also be given if there is a positive fluid balance of 1.5 litres, a weight gain of 1.5kg or symptoms of fluid overload. The patient should be asked to drink 2 litres of fluid in the 24hrs following treatment, and to contact the hospital if this is impossible because of problems e.g. nausea and vomiting.

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 cisplatin and pemetrexed may be considered. If in doubt, discuss with Consultant.

Renal Impairment: NB. Cisplatin is both eliminated primarily (> 90%) in the urine and is itself nephrotoxic.

GFR (ml/min)	Cisplatin Dose
≥ 60	Give 100%
45 – 59	Give 75%
< 45	CI (consider carboplatin)

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

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

Neurotoxicity: Grade 2 neurotoxicity requires a 50% dose reduction of cisplatin. For Grade 3 or 4 neurotoxicity, treatment should be discontinued.

Other Toxicities:

	Dose of Pemetrexed	Dose of Cisplatin
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)
Scagliotti, GV et al; JCO 2008; 26 (21): 3543 – 3551 (NSCLC)