PEMETREXED

Maintenance treatment of locally advanced or metastatic NSCLC, other than predominantly squamous cell histology, if disease has not progressed immediately following platinum-based chemotherapy:

a) Maintenance following 1st line platinum plus gemcitabine, paclitaxel or docetaxel (NICE 2010)

b) Maintenance following 1st line cisplatin plus pemetrexed x 4 cycles (NICE 2016)
Blueteq registration is required before maintenance treatment may start in this setting

Drugs/Dosage:	Pemetrexed 500mg/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 pemetrexed 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 3 days, commencing the morning of the day prior to chemotherapy
Administration:	in 100ml sodium chloride 0.9%, infused over 10 minutes
Frequency:	3 weekly until disease progression
Main Toxicities:	myelosuppression; mucositis; skin rash; renal toxicity; ovarian failure / infertility
Anti-emetics:	mildly emetogenic
Extravasation:	non vesicant
Regular Investigations:	FBC Day 1 U&Es Day 1 (watch renal function closely) LFTs Day 1 EDTA prior to 1st cycle, only if not measured during 1st line chemotherapy CT scan every 3 months
Comments:	**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 treatment, with dose adjusted as below:

If nadir neutrophils < 0.5 x 10^9/L or nadir platelets < 50 x 10^9/L (and no bleeding), give 75% of previous dose for subsequent cycles.
If nadir platelets < 50 x 10^9/L and bleeding, give 50% of previous dose for remaining cycles.

Renal Impairment: Re-check serum creatinine and monitor CrCl before each dose is given, as renal function may occasionally deteriorate to below the threshold for continued treatment:

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

Hepatic Impairment: Pemetrexed is primarily renally excreted unchanged. However, patients with bilirubin > 1.5 x ULN or ALT/AST > 3 x ULN (liver metastases absent) or > 5 x ULN (liver metastases present) have not been studied.

Other Toxicities:

	Dose of Pemetrexed
Grade 3 or 4 mucositis	Give 50% **of previous dose**
Any other Grade 3 or 4 toxicities, or any diarrhoea requiring hospitalisation	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: Ciuleanu, Proceedings of ASCO 2008; Abstract #8011 ("switch" maintenance)
Paz-Ares, L et al; Lancet Oncology 2012; 13 (3): 247 - 255 (Paramount study)