LONDON CANCER ALLIANCE West and South

Lung Pathway Group – Pemetrexed in Non-Small Cell Lung Cancer (NSCLC)

Indication:	
NICE TA190	Maintenance treatment for locally advanced or metastatic **non-squamous** NSCLC not previously treated with pemetrexed and cisplatin as first treatment. Disease which has not progressed immediately following platinum-based chemotherapy in combination with gemcitabine, paclitaxel or docetaxel Pemetrexed should not be started sooner than 3 weeks following previous chemotherapy, or 4 weeks following radiotherapy
NCDF criteria	Maintenance treatment of advanced **non-squamous** NSCLC following 1st line chemotherapy with cisplatin and pemetrexed not progressing after 4 cycles. PS 0 or 1
Regimen details:	Pemetrexed 500 mg/m^2 IV Day 1
Administration:	Pemetrexed in 100ml Sodium Chloride 0.9% over 10 minutes
Frequency:	Day 1, every 21 days until disease progression or unacceptable toxicities
Pre-medication:	Oral dexamethasone 4mg BD for 3 days, starting the day prior to chemotherapy (to reduce incidence / severity of skin reactions as well as anti-emetic role). In exceptional circumstances when dexamethasone pre-medication has been omitted the day before treatment, this can be replaced with dexamethasone 8mg IV administered one hour before treatment.
Anti- emetics:	Low emetogenicity Follow Local Anti-emetic Policy

Version: 1.0 Supersedes: all other versions	Approved by LCA Lung Pathway Chemotherapy Lead: Rohit Lal
Reason for Update: LCA Protocol Development	Approved by LCA Joint Delivery Subgroup Co-Chairs: Pauline McCalla & Rebecca Johl
Prepared by: Lisa Yuen	Approved by LCA Medicines & Chemotherapy Steering Group Chair:
Second check by: Laura Cameron	Date prepared: November 2014 Review Date: November 2016

Supportive medication: Folic acid 400micrograms orally once a day starting at least 5 days before first treatment and continuing until 3 weeks after the last pemetrexed dose.
Vitamin B_{12} (hydroxocobalamin) 1000micrograms by IM injection, start the week before first treatment, then once every 9 weeks (can be given on same day as pemetrexed) until 3 weeks after last pemetrexed dose.
Mouthcare as per local policy

Extravasation: Non-vesicant

Regular investigations:

Prior to Cycle 1:

FBC	Day 1 (within 14 days)
LFTs	Day 1 (within 14 days)
U&Es	Day 1 (within 14 days)
CT Scan	Baseline

Prior to Day 1 (all cycles):

FBC	Day 1 (within 72 hours)
LFTs	Day 1 (within 72 hours)
U&Es	Day 1 (within 72 hours)
Imaging	After 3 cycles

Toxicities: Myelosuppression, skin rash, mucositis, diarrhoea, alopecia (mild), ovarian failure/infertility, nausea/vomiting, loss of appetite, thrombocytopenia, neurotoxicity, fatigue

DOSE MODIFICATIONS

Haematological Toxicity

Neutrophils (x 10^9/L)		Platelets (x 10^9/L)	Dose
≥ 1.5	**&**	≥ 100	100% dose
≤ 1.5	**&/or**	≤ 100	Delay for 1 week. Repeat FBC, if recovered to above these levels, give 100% dose. For > 2 delays, a 25% dose reduction may be considered – discuss with the Consultant.

Non-haematological Toxicities

Renal Impairment

Creatinine Clearance (ml/min)	Pemetrexed Dose
≥ 45	Give 100% dose
< 45	Not recommended – discuss with Consultant

Hepatic Impairment

Bilirubin	ALP, ALT, AST	Pemetrexed Dose
≤ 1.5 x ULN	≤ 3 x ULN or ≤ 5 x ULN if liver involvement	Give 100% dose

No information is available on dose reduction for pemetrexed in more severe hepatic impairment - discuss with consultant

Dose modifications for other toxicities as appropriate

Neurotoxicity	Pemetrexed Dose
Grade 2	Give 100% dose
Grade 3 or 4	Discontinue

Other toxicities

	Pemetrexed Dose
Any grade 2 toxicity	Give 100% dose
Grade 3 or 4 mucositis	Withhold until resolves then give 50% of previous dose
Any grade 3 or 4 toxicities (except mucositis)	Withhold until resolves, then give 75% of previous dose
Diarrhoea (any grade) requiring hospitalisation	Withhold until resolves, then give 75% of previous dose

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

Location of regimen: delivery — Day case setting

Comments: Women of childbearing potential must use effective contraception during treatment
Sexually mature males are advised not to father a child during the treatment, and up to 6 months thereafter.
If appropriate, male patients should be advised to seek counselling on sperm storage before starting treatment.

Drug interactions: Nephrotoxic drugs

Concomitant administration of substances that are also tubularly secreted

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

Live vaccines

Concomitant yellow fever vaccine is contra-indicated

Increased monitoring of INR levels is required with oral anticoagulants

Cases of radiation pneumonitis have been reported in patients treated with radiation either prior, during, or subsequent to their pemetrexed therapy. Particular attention should be paid to these patients, and caution exercised with use of other radiosensitising agents.

References:

NICE TA190

Ciuleanu et al. (2009) The Lancet,374:1432-1440

www.medicines.org.uk