LONDON CANCER ALLIANCE West and South

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

Indication:	Advanced or metastatic **non-squamous** NSCLC (histology confirmed as adenocarcinoma or large cell carcinoma) where cisplatin is not a suitable treatment option. Performance status 2+			
Regimen details:	Pemetrexed	500 mg/m^2	IV	Day 1
	Carboplatin	AUC 5	IV	Day 1
Administration:	Pemetrexed in 100ml Sodium Chloride 0.9% over 10 minutes 30 minutes after pemetrexed infusion: Carboplatin in 500ml Glucose 5% over 60 minutes Aluminium containing equipment should not be used during preparation and administration of carboplatin Hypersensitivity reactions may occur, such as flushing, rash with or without pruritus, chest tightness, back pain, dyspnoea and fever or chills, usually during the first and second infusions and within a few minutes following the start of the infusion; the infusion should be slowed down or interrupted and the necessary supportive medication should be administered. Severe reactions such as hypotension and/or bronchospasm or generalised rash/erythema requires immediate discontinuation. Availability of resuscitation equipment must be ensured as a standard precaution.			
Frequency:	Day 1, every 21 days, for up to 6 cycles			
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).			

Version: 1.0 Supersedes: all other versions	Approved by LCA Lung Pathway Chemotherapy Lead: Dr 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: Jamie Ferguson
Second check by: Laura Cameron	Date prepared: November 2014 Review Date: November 2016

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: High emetogenicity
Follow Local Anti-emetic Policy

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.
Paracetamol / Chlorphenamine / Hydrocortisone can be given for administration-related reactions such as chills / fever.
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)
EDTA	See comments
CT scan	Baseline

Comments:
Carboplatin dose should be calculated using the Calvert formula: Dose = Target AUC x (25 + GFR). GFR should be calculated using EDTA clearance before prescribing. (If EDTA not available prior to cycle 1, initiate treatment using the Cockcroft & Gault formula to calculate GFR, and ensure EDTA prior to cycle 2).
Monitor trends in serum creatinine between treatments, if >25% from baseline value re-calculate GFR using the Cockcroft & Gault formula or EDTA.

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, alopecia (mild), mucositis, diarrhoea, ovarian failure/infertility, nausea / vomiting, thrombocytopenia,

neurotoxicity and ototoxicity - risk increased if previously treated with cisplatin

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 >1 delay, a 25% dose reduction of both carboplatin and pemetrexed may be considered – discuss with the Consultant.

Non-haematological Toxicities

Renal Impairment

Creatinine Clearance (ml/min)	Pemetrexed Dose	Carboplatin Dose
≥ 45	Give 100% dose	Give 100% dose
< 45	Not recommended – discuss with Consultant	Give 100% dose
< 20		Contraindicated

Hepatic Impairment

Carboplatin No dose modifications required

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

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

Neurotoxicity	Pemetrexed Dose	Carboplatin Dose
Grade 2	Give 100% dose	Give 50% dose
Grade 3 or 4	Discontinue	Discontinue

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Other toxicities

	Pemetrexed Dose	**Carboplatin Dose**
Any grade 2 toxicity	Give 100% dose	Give 100% dose
Any grade 3 toxicities (except mucositis)	Give 75% of previous dose	Give 75% of previous dose
Any grade 4 toxicities (except mucositis)	Give 75% of previous dose	Give 50% of previous dose
Diarrhoea (any grade) requiring hospitalisation	Give 75% of previous dose	Give 75% of previous dose
Grade 3 mucositis	Give 50% of previous dose	Give 75% of previous dose
Grade 4 mucositis	Give 50% of previous dose	Give 50% 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:
Phenytoin
Nephrotoxic drugs
Aminoglycoside antibiotics-increased risk of ototoxicity
Non-steroidal anti-inflammatory drugs should be avoided from 5 days before each dose of pemetrexed until 2 days after each dose.
Live vaccines
Concomittant yellow fever vaccine is contra-indicated
Increased monitoring of INR levels is required with anticoagulants

References: Scagliotti et al. (2008): JCO, Vol 26(21)

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