Pemetrexed and Carboplatin in Non Small Cell lung cancer: PemCarb

**Indication:**
Locally advanced or metastatic Non Small Cell lung cancer (NSCLC), when Cisplatin is not suitable treatment option.
Histology of the tumour confirmed as Non-squamous cell type (Adenocarcinoma or Large-cell carcinoma)

**Regimen details:**
Pemetrexed 500mg/m² IV D1
Carboplatin AUC 5 (See comments) IV D1
(Carboplatin AUC 6 if dose calculated using Cockroft&Gault equation)

**Administration:**
Pemetrexed in 100ml Sodium Chloride 0.9% IV over 10 minutes
Then, 30 minutes after end of Pemetrexed administration:
Carboplatin in 500ml Glucose 5% IV over 60 minutes

**Premedication:**
Dexamethasone 4mg BD for 5 days, commencing the morning of 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.

**Frequency:**
3 weekly for up to 6 cycles, dependent on subjective and objective response

**Extravasation:**
Non vesicants

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

**Supportive medication:**
Folic acid 400mcg po od starting at least 5 days before first treatment and continuing until 3 weeks after the last pemetrexed dose
Vitamin B12 1000mcg 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

**Regular investigations:**
FBC D1
LFTs & U&Es D1
EDTA Prior to 1st cycle (see Comments)
CXR Before each cycle
CT scan Prior to 1st cycle and after Cycle 2

**Comments:**
Carboplatin dose should be calculated using the Calvert formula:
Dose = Target AUC x (25 + GFR)
GFR should be calculated using the Cockcroft & Gault equation in all patients; if the calculated GFR < 60 or >120ml/min measure EDTA clearance or creatinine clearance before prescribing. Carboplatin dose is calculated as AUC5 if EDTA is used. Monitor trends in serum creatinine between treatments: if >25% from baseline value re-calculate GFR using the Cockcroft & Gault equation.
**Dose Modifications**

### Haematological Toxicity

<table>
<thead>
<tr>
<th>Condition</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophils &lt; 1.5 x 10^9/l</td>
<td>Delay for 1 week.</td>
</tr>
<tr>
<td>or</td>
<td>Repeat FBC –</td>
</tr>
<tr>
<td>Platelets &lt; 100 x 10^9/l</td>
<td>If within normal parameters, resume treatment with 100% doses. If 2 or more delays, a 25% dose reduction of both Carboplatin and Pemetrexed may be considered. If in doubt, discuss with Consultant.</td>
</tr>
</tbody>
</table>

### Hepatic Impairment

Carboplatin: No dose adjustments indicated.

Recommended hepatic test results for **Pemetrexed**:

- **Bilirubin**: ≤1.5-times upper limit of normal
- **AST, ALP, ALT**: ≤3-times upper limit of normal
- **AST, ALP, ALT**: ≤5-times upper limit of normal is acceptable if liver has tumour involvement.

No information is available on dose reduction for pemetrexed in more severe hepatic impairment.

### Renal Impairment

<table>
<thead>
<tr>
<th>CrCl (ml/min)</th>
<th>Pemetrexed Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥45</td>
<td>Give 100% dose</td>
</tr>
<tr>
<td>&lt;45</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>

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

### Other toxicities

<table>
<thead>
<tr>
<th>Grade 3 or 4 mucositis</th>
<th>Dose of Pemetrexed</th>
<th>Dose of Carboplatin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Give 50% of previous dose</td>
<td>Give 100% of previous dose</td>
</tr>
</tbody>
</table>

Any other Grade 3 or 4 toxicities, or any diarrhoea requiring hospitalisation

<table>
<thead>
<tr>
<th>Dose of Pemetrexed</th>
<th>Dose of Carboplatin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Give 75% of previous dose</td>
<td>Give 75% of previous dose</td>
</tr>
</tbody>
</table>

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

**Common Toxicities:**

- Myelosuppression; Skin rash; Alopecia (mild); Mucositis; Diarrhoea; Ovarian failure/Infertility; Nausea/ Vomiting, Thrombocytopenia, Neurotoxicity and ototoxicity- risk increased if previously treated with Cisplatin

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:**

- NICE FAD, Aug-09
- [www.medicines.org.uk](http://www.medicines.org.uk), accessed Aug-09
- Micromedex review, accessed Aug-09
- Scagliotti et al. (2008): JCO, Vol 26(21)