# Regimen: Carboplatin + Etoposide for small cell lung cancer

**ICD10 codes**
Codes pre-fixed with C34.

**Indication**
First line chemotherapy for patients with small cell lung cancer

<table>
<thead>
<tr>
<th>Regimen details</th>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>Carboplatin</td>
<td>AUC 5¥</td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Etoposide</td>
<td>100mg/m²</td>
<td>IV</td>
</tr>
<tr>
<td>2 and 3</td>
<td>2</td>
<td>Etoposide</td>
<td>100mg/m²</td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>OR</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Etoposide</td>
<td>200mg/m²</td>
<td>PO</td>
</tr>
</tbody>
</table>

¥ Calculate Carboplatin dose using Calvert equation:
Carboplatin dose (mg) = AUC (GFR + 25)

Generally the Cockcroft Gault calculation can be used to calculate creatinine clearance. However care should be taken if creatinine level is not felt to truly reflect renal function as in extremes of BSA or in debilitated patients. Creatinine clearance should be capped at 125ml/min for carboplatin dosing as recommended by the US FDA. Consider EDTA clearance.

**Administration**

**Day 1**
Carboplatin diluted in 500ml 5% Glucose over 30 minutes.
Etoposide IV diluted in 1 litre of 0.9% Sodium Chloride and infused over a minimum of 1 hour.

**Days 2 and 3:** Etoposide if given IV is given in 1000ml Sodium Chloride 0.9% over 1 hour.
If taken orally (oral absorption is variable), the oral Etoposide dose is to be rounded to nearest 50mg, and swallowed whole on an empty stomach or an hour before food. In the event that the patient cannot swallow etoposide capsules, etoposide injection can be taken orally (diluted with orange juice immediately prior to administration) at a dose of 70% of the usual oral capsule dose on Day 2 and Day 3. (This is an unlicensed use based on medical information from Bristol-Myers Squibb).

**Frequency**
Every 3 weeks for 4-6 cycles (Usually 4)

**Extravasation**
Carboplatin is an irritant (group 3)
Etoposide is an irritant (group 3)

**Premedication**
Antiemetics as per local protocol.

**Emetogenicity**
This regimen has moderate emetogenic potential – refer to local protocol

**Additional recommended supportive medication**
Patients with poor performance status or age > 70 years should be considered for prophylactic ciprofloxacin, 250mg twice daily for 7 days and fluconazole 50mg od, starting on Day 7, to cover the nadir.

**Pre-treatment evaluation**
FBC
U+E
LFT
Baseline radiology CXR plus CT scan of chest and upper abdomen.

Baseline – results valid for 14 days
Baseline – results valid for 14 days
Baseline – results valid for 14 days

**Regular investigations**
FBC
U+E
LFT
CXR or CT scan every 2

Results valid for 72 hours
Results valid for 72 hours
Results valid for 7 days

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### Standard limits for administration to go ahead

- **Neutrophil count**: $\geq 1.5 \times 10^9/L$
- **Platelet count**: $\geq 100 \times 10^9/L$
- **Bilirubin**: $\leq 1.5 \times \text{ULN}$
- **AST/ALT**: $\leq 1.5 \times \text{ULN}$
- **Alk Phos**: $\leq 2.5 \times \text{ULN}$

### Dose modifications

Consider AUC 4 for patients with poor performance status.

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Neutrophils $\times 10^9/L$</th>
<th>Platelets</th>
<th>Dose reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1.5</td>
<td>or</td>
<td>&lt; 100</td>
<td>Delay for 1 week. Repeat FBC and, if within normal parameters, resume treatment.</td>
</tr>
</tbody>
</table>

If significant myelosuppression, consider reduction of oral etoposide dose to 100mg/m² on Day 2 and Day 3. The use of prophylactic G-CSF should be discussed with the consultant.

### Renal Impairment

Carboplatin is contraindicated if CrCl $\leq 20$ ml/min.

If the calculated GFR falls by $>10\%$ from previous cycle, consider dose recalculation. If calculated GFR appears to improve the dose should not be increased unless a clear cause of renal function improvement is documented (e.g. treatment of urinary tract obstruction).

<table>
<thead>
<tr>
<th>CrCl (ml/min)</th>
<th>Etoposide Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>$&gt; 50$</td>
<td>Give 100%</td>
</tr>
<tr>
<td>$15 - 50$</td>
<td>Give 75%</td>
</tr>
<tr>
<td>$&lt; 15$</td>
<td>Give 50%</td>
</tr>
</tbody>
</table>

### Hepatic Impairment

<table>
<thead>
<tr>
<th>Bilirubin Micromol/L</th>
<th>AST/ALT $\times \text{ULN}$</th>
<th>Carboplatin</th>
<th>Etoposide</th>
</tr>
</thead>
<tbody>
<tr>
<td>$&lt; 26$</td>
<td>and $&lt; 5$</td>
<td>Full</td>
<td>Full</td>
</tr>
<tr>
<td>$26 - 50$</td>
<td>or $&lt; 5$</td>
<td>Full</td>
<td>50%</td>
</tr>
<tr>
<td>$\leq 50$</td>
<td>and $&gt; 5$</td>
<td>Full</td>
<td>25% or omit*</td>
</tr>
<tr>
<td>$51 - 68$</td>
<td>and $&lt; 5$</td>
<td>Full</td>
<td>25% or omit*</td>
</tr>
<tr>
<td>$&gt; 68$</td>
<td></td>
<td>Omit/delay</td>
<td>Omit/delay</td>
</tr>
</tbody>
</table>

*The decision to treat should be confirmed by a consultant.

### NCI Common toxicity criteria

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any grade 3-4 toxicities besides mucositis and alopecia</td>
<td>25% dose reduction of carboplatin and etoposide after recovery to $\leq$ grade 1</td>
</tr>
</tbody>
</table>

### Adverse effects –

the contents of the table indicate the adverse effects that should be documented on consent to treatment forms

<table>
<thead>
<tr>
<th>Rare or serious side effects</th>
<th>Frequently occurring side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myelosuppression</td>
<td>Alopecia</td>
</tr>
<tr>
<td></td>
<td>Nausea and vomiting</td>
</tr>
<tr>
<td></td>
<td>Electrolyte disturbances</td>
</tr>
</tbody>
</table>

### Significant drug interactions – For full details consult product literature/reference texts

| Significant drug interactions | Phenybutazone, sodium salicylate and salicylic acid can affect protein binding of etoposide. |

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Comments

For SCLC patients with limited stage disease and good performance status, concomitant radiotherapy may be administered with one of the cycles as follows:
40Gy in 15 fractions (2.67Gy/#) over 3 weeks, on weekdays only.
This is usually initiated on Day 1 of the 2nd or 3rd cycle of chemotherapy. Radiotherapy is to be given after chemotherapy on Day 1 of the cycle. Radiotherapy may also be administered sequentially after completion of chemotherapy for patients with limited stage disease and contraindications to concurrent treatment.
Consider prophylactic cranial irradiation after completion of chemotherapy.

Cumulative Doses

References

- CONVERT trial protocol, v3 10June 2008