# Carboplatin and Etoposide (lung)

## Indication

First line chemotherapy for patient with small cell lung cancer (SCLC), when cisplatin is not appropriate.

Re-challenge as second line therapy for patients who have previously responded to platinum and etoposide.

## ICD-10 codes

Codes pre-fixed with C34

## Regimen details

| Day | Drug | Dose | Route |
|---|---|---|---|
| 1 | Carboplatin | AUC5* | IV infusion |
| 1 | Etoposide | 100mg/m² | IV infusion |
| 2 and 3 **or** | Etoposide | 100mg/m² | IV infusion |
| 2 and 3 | Etoposide | 200mg/m² | PO |

* Carboplatin dose calculated using the Calvert equation: **Carboplatin dose (mg) = AUC (CrCl +25)**
The creatinine clearance (CrCl) is calculated using the Cockcroft and Gault equation, however for patients where the creatinine level may not truly reflect renal function (e.g. in extremes of BSA or debilitated patients) an EDTA should be performed.
CrCl should be capped at 125mL/min

## Cycle frequency

21 days

## Number of cycles

4 - 6 cycles (usually 4)

## Administration

**Day 1**
Carboplatin is administered in 500mL 5% glucose over 30 minutes.

Etoposide is administered in 1000mL sodium chloride 0.9% and infused over a minimum of 1 hour.

**Days 2 and 3**
IV etoposide is administered in 1000mL sodium chloride 0.9% and infused over a minimum of 1 hour.

Oral etoposide is available as 50mg and 100mg capsules. The dose should 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 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 days 2 and 3. (This is an unlicensed use based on medical information from Bristol- Myers Squibb).
Note: oral absorption of etoposide is variable.

## Pre-medication

Antiemetics as per local guidelines.

## Emetogenicity

This regimen has moderate emetic potential.

## Additional supportive medication

Consider prophylactic ciprofloxacin 250mg BD and fluconazole 50mg OD for 7 days, starting on day 7, for patients with extensive disease, poor performance status or age >70 years.

## Extravasation

Carboplatin and etoposide are irritant (Group 3)

## Investigations – pre first cycle

| **Investigation** | **Validity period** (or as per local policy) |
|---|---|
| FBC | 14 days |
| U+E (including creatinine) | 14 days |
| LFTs | 14 days |

## Investigations – pre subsequent cycles

| **Investigation** | **Validity period** (or as per local policy) |
|---|---|
| FBC | 96 hours |
| U+E (including creatinine) | 7 days |
| LFTs | 7 days |

## Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

| **Investigation** | **Limit** |
|---|---|
| Neutrophils | ≥1.0 x $10^9$/L |
| Platelets | ≥100 x $10^9$/L |
| Bilirubin | ≤1.5 x ULN |
| ALT/AST | ≤1.5 x ULN |
| Alkaline phosphatase | ≤2.5 x ULN |
| Sodium | ≥130 x $10^9$/L (if < 130 – discuss with consultant) |
| Creatinine Clearance (CrCl) | >50mL/min |

## Dose modifications

Consider reducing carboplatin dose to AUC 4 for patients with poor performance status.

- ### Haematological toxicity

Defer therapy for 1 week if neutrophils < 1.0 x $10^9$/L or platelets < 100 x $10^9$/L. If repeat FBC within range continue with treatment.

If significant myelosuppression consider reducing oral etoposide dose to 100mg/$m^2$ on days 2 and 3. Consider prophylactic GCSF support.

- ### Renal impairment

| **CrCl** (mL/min) | **Etoposide dose** |
|---|---|
| >50 | 100% |
| 15-50 | 75% |
| <15 | 50% |

Carboplatin is contraindicated if CrCl <20mL/min.

If the calculated creatinine clearance falls by >10% from previous cycle recalculate dose of carboplatin. If the calculated creatinine clearance 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).

- **Hepatic impairment**

| **Bilirubin** (x ULN) | | **AST/ALT** (x ULN) | **Etoposide dose** |
|---|---|---|---|
| <1.5 | and | < 1.5 | 100% |
| 1.5-3.0 | or | 1.5-3.0 | 50% |
| >3.0 | or | > 3.0 | 25% or omit (consultant decision) |

No dose modification required for carboplatin.

- **Other toxicities**

Any Grade 3-4 toxicity (except mucositis and alopecia) – delay until ≤ grade 1 toxicity and reduce doses of carboplatin and etoposide to 75%.

## Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Neuropathy
Hypersensitivity reactions
Nephrotoxicity

- **Frequently occurring side effects**

Myelosuppression
Alopecia
Nausea and vomiting
Electrolyte disturbances

- **Other side effects**

Rash
Flu like illness
Abnormal LFTs

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

**Phenylbutazone, sodium salicylate and salicylic acid:** can affect protein binding of etoposide.

**Warfarin/coumarin anticoagulants:** increased or fluctuating anticoagulant effects. Avoid if possible, consider switching patient to a low molecular weight heparin during treatment or if the patient continues taking an oral anticoagulant monitor the INR at least once a week and adjust dose accordingly.

**Carboplatin only:**
**Aminoglycoside antibiotics:** increased risk of nephrotoxicity and ototoxicity
**Clozapine:** increased risk of agranulocytosis, avoid concomitant use
**Diuretics:** increased risk of nephrotoxicity and ototoxicity
**Nephrotoxic drugs**: increased nephrotoxicity ; not recommended
**Phenytoin:** carboplatin reduces absorption and efficacy of phenytoin

## Additional comments

For patients with limited stage disease and good performance status, concomitant radiotherapy may be administered to start with cycle 2.

## References


- Summary of Product Characteristics Carboplatin (Hospira) accessed 25 Sept 2014 via www.medicines.org.uk
- Summary of Product Characteristics Etoposide (Bristol Myers Squibb) accessed 25 Sept 2014 via www.medicines.org.uk
- Skarlos, DV., et al. Randomised comparison on etoposide-cisplatin v etoposide-carboplatin in SCLC. Ann Onc. (1994) 5 (7) 601-607.
- The North London Cancer Network. Dose adjustments in renal impairment. January 2009.



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