# CISplatin (75mg/m$^2$) + Etoposide (100mg/m$^2$) +Thoracic Radiotherapy (TRT) -21 day

## INDICATIONS FOR USE:

| INDICATION | ICD10 | Regimen Code | *Reimbursement Indicator |
|---|---|---|---|
| Small cell lung cancer (SCLC) limited disease | C34 | 00279a | |

*If a reimbursement indicator (e.g. ODMS, CDS[1]) is not defined, the drug and its detailed indication have not gone through the formal reimbursement process as legislated for in the Health (Pricing and Supply of Medical Goods) Act 2013.*

## TREATMENT:

*The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.*

CISplatin is administered on day 1 and etoposide is administered on three consecutive days (Days 1-3) of a 21day cycle for 4 cycles.

Facilities to treat anaphylaxis MUST be present when the chemotherapy is administered.

Usual plan is for radiotherapy to start with the first cycle of chemotherapy, although radiotherapy may be started with later cycles dependent on clinical circumstances.

Regimen may be administered every 28 days at discretion of prescribing consultant.

| Admin Order | Day | Drug | Dose | Route | Diluent & Rate |
|---|---|---|---|---|---|
| 1 | 1, 2 & 3 | Etoposide | 100mg/m$^2$ | IV Infusion | 1000ml 0.9% NaCl over 60mins |
| 2 | 1 | CISplatin | [a]75mg/m$^2$ | IV Infusion | 500-1000ml NaCl 0.9% over 2 hours (Pre and Post hydration therapy required)[b] |

[a]The total dose of CISplatin may be fractionated and given over 3 days i.e. 25mg/m$^2$ on day 1

[b]Pre and post hydration therapy required for CISplatin
See local hospital policy recommendations.
Suggested prehydration for CISplatin therapy:

1. Administer 10mmol magnesium sulphate ($MgSO_4$) in 1000 mL sodium chloride 0.9% over 60 minutes.
2. Administer 200 mL of mannitol 20% over 15 minutes*(near the completion of the first bag of hydration fluids) (mannitol should be administered via a controlled infusion)

Administer CISplatin as described above
Post hydration: Administer 1000ml 0.9% NaCl over 60mins

*Mannitol 10% may be used as per institutional policy; there is much variation in the use of mannitol and although there is no conclusive evidence that mannitol should be used.

In cases of CISplatin toxicity or poorly functioning patients or age > 75 CARBOplatin AUC 5 **(Dose = AUC x (GFR* +25) )** administered on Day 1 only may be substituted.

## ELIGIBILTY:

- Indications as above
- ECOG status 0-2
- Suitable candidate for thoracic radiation

## EXCLUSIONS:

- Hypersensitivity to etoposide, CISplatin or any of the excipients.
- CISplatin
  - Pre existing neuropathies ≥ grade 2
  - Creatinine clearance < 60 mL/min
  - Significant hearing impairment/tinnitus
- Severe liver impairment (etoposide)
- Pregnancy
- Breast Feeding

## PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist.

## TESTS:

**Baseline tests**:

- Blood, renal and liver profile
- Audiology and creatinine clearance if clinically indicated

**Regular tests**:

- Blood, renal and liver profile prior to each cycle

**Disease monitoring:**

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

## DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant

**Haematological:**

**Table 1: Dose modification of ETOPOSIDE for haematological toxicity**

| ANC (x $10^9$/L) | | Platelets (x $10^9$/L) | Dose Etoposide |
|---|---|---|---|
| ≥ 1.5 | **and** | ≥ 100 | 100% |
| 1-1.49 | **or** | 75-99 | 75% |
| < 1 | **or** | < 75 | DELAY |

**Renal and Hepatic Impairment:**

**Table 2: Dose modification in renal and hepatic impairment**

| Drug | Renal impairment | | Hepatic Impairment | | | |
|---|---|---|---|---|---|---|
| **Etoposide** | **Cr Cl (ml/min)** | **Dose** | **Bilirubin (micromol/L)** | | **AST (Units/L)** | **Dose Etoposide** |
| | >50 | 100% | 26-51 | or | 60-180 | *50% |
| | 15-50 | 75% | >51 | or | >180 | Clinical decision |
| | Subsequent dosing should be based on patient tolerance and clinical effect. Data are not available in patients with CrCl < 15ml/min and further dose reductions should be considered in these patients. | | | | | |
| **CISplatin** | **GFR (ml/min)** | **Dose of CISplatin** | **No dose reduction necessary** | | | |
| | ≥ 60 | 100% | | | | |
| | 45-59 | 75% | | | | |
| | <45 | Consider CARBOplatin /Clinical decision | | | | |

**Non-Haematological Toxicity:**

**Table 3: Dose modification schedule based on adverse events**

| Adverse reactions | Discontinue | Recommended dose modification |
|---|---|---|
| Grade ≥ 2 peripheral neuropathy | | Substitute CARBOplatin AUC 5 or 50% reduction of CISplatin dose after recovery to grade ≤ 1;<br>100% dose of etoposide. |
| Grade 3 (Other than mucositis or alopecia) | | Delay until recovery to Grade 1.<br>Then reduce dose of CISplatin and etoposide to 75%. |

## SUPPORTIVE CARE:

### EMETOGENIC POTENTIAL:

**CISplatin** High
**Etoposide** Low (**Refer to local policy).**

### PREMEDICATIONS:

Hydration prior and post CISplatin administration **(Reference local policy or see recommendations above).**

### OTHER SUPPORTIVE CARE:

No specific recommendations

## ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

*The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.*

- **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated appropriately. Avoid aminoglycoside antibiotics.
- **Renal Toxicity**: Nephrotoxicity is common with CISplatin. Strongly encourage oral hydration. If oral

hydration is not possible (e.g. excessive nausea), IV hydration is indicated. Avoid nephrotoxic drugs such as aminoglycoside antibiotics where possible. Where treatment with nephrotoxic drugs must be used, monitor renal function.

- **Ototoxicity and sensory neural damage**: These are associated with CISplatin therapy. They should be assessed by history prior to each cycle.
- **Hypersensitivity:** Hypersensitivity reactions have been reported with etoposide and CISplatin. Monitor infusion of etoposide for the first 15 minutes for signs of hypotension.

## DRUG INTERACTIONS:

- CISplatin may potentiate the nephrotoxic and ototoxic effects of loop diuretics and aminoglycosides so concurrent use should be avoided.
- Concomitant CISplatin therapy is associated with reduced total body clearance of etoposide.
- CYP3A4 inducers may increase the clearance of etoposide.
- CYP3A4 and p-gp inhibitors may decrease the clearance of etoposide
- Current drug interaction databases should be consulted for more information

## ATC CODE:

| | |
|---|---|
| CISplatin | L01XA01 |
| Etoposide | L01CB01 |

## REFERENCES:


1. Turrisi AT, Kim K, Blum R et al. Twice-Daily Compared with Once-Daily Thoracic Radiotherapy in Limited Small-Cell Lung Cancer Treated Concurrently with CISplatin and Etoposide N Engl J Med 1999; 340:265-271
2. Park K, Sun J, Kim, S. et al. Phase III trial of concurrent thoracic radiotherapy (TRT) with either the first cycle or the third cycle of CISplatin and etoposide chemotherapy to determine the optimal timing of TRT for limited-disease small cell lung cancer. J Clin Oncol 2012 (suppl; abstr 7004)
3. CISplatin 1mg/ml Concentrate for Solution for Infusion. Summary of Product Characteristics Accessed July 2017. Available at http://www.hpra.ie/img/uploaded/swedocuments/LicenseSPC_PA0749-119-002_06062013115044.pdf
4. Etoposide 20 mg/ml Concentrate for Solution for Infusion Summary of Product Characteristics Accessed July 2017 Available at http://www.hpra.ie/img/uploaded/swedocuments/LicenseSPC_PA1809-020-001_07102015115038.pdf


| Version | Date | Amendment | Approved By |
|---|---|---|---|
| 1 | 10/09/2015 | | Dr Maccon Keane |
| 2 | 20/09/2017 | Updated title and dosing in renal impairment, applied new NCCP regimen template | Prof Maccon Keane |
| | | | |

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

[i] ODMS – Oncology Drug Management System
CDS – Community Drug Schemes (CDS) including the High Tech arrangements of the PCRS community drug schemes
Further details on the Cancer Drug Management Programme is available at;
http://www.hse.ie/eng/services/list/5/cancer/profinfo/medonc/cdmp/