

CISplatin (75mg/m²) + Etoposide (100mg/m²) +Thoracic Radiotherapy (TRT) -21 day

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement status
Small cell lung cancer (SCLC) limited disease	C34	00279a	Hospital

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 21 day 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	Cycle
1	1, 2 & 3	Etoposide	100mg/m ²	IV Infusion	1000ml 0.9% NaCl over 60mins	Every 21 days for 4 cycles
2	1	CISplatin ^b	^a 75mg/m ²	IV Infusion	1000ml 0.9% NaCl over 2 hours	Every 21 days for 4 cycles

^aThe total dose of CISplatin may be fractionated and given over 3 days i.e. 25mg/m² on day 1

^bPre and post hydration therapy required for CISplatin

See local hospital policy recommendations.

Suggested prehydration for CISplatin therapy:

- Administer 10mmol magnesium sulphate (MgSO₄) ((+/-KCl 20mmol/L if indicated) in 1000 mL sodium chloride 0.9% over 60 minutes.

Administer CISplatin as described above

Post hydration: Administer 1000 ml 0.9% NaCl over 60mins

Mannitol 10% may be used to as per local policy to induce diuresis, although there is no conclusive evidence that this is required. The routine use of furosemide to increase urine flow is not recommended unless there is evidence of fluid overload.(2,3)

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.

ELIGIBILITY:

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

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EXCLUSIONS:

- Hypersensitivity to etoposide, CISplatin or any of the excipients.
- CISplatin
 - Pre existing neuropathies \geq 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 ($\times 10^9$ /L)		Platelets ($\times 10^9$ /L)	Dose Etoposide
≥ 1.5	and	≥ 100	100%
1-1.49	or	75-99	75%
< 1	or	< 75	DELAY

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Renal and Hepatic Impairment:

Table 2: Dose modification in renal and hepatic impairment

Drug	Renal impairment		Hepatic Impairment			
Etoposide	CrCl (ml/min)	Dose	Bilirubin (micromol/L)		AST (Units/L)	Dose
	>50	100%	26-51	or	60-180	50%
	15-50	75%	>51	or	>180	Clinical decision
	<15	50%				
Subsequent dosing should be based on patient tolerance and clinical effect.						
CISplatin	CrCl (ml/min)	Dose	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	Recommended dose modification
Grade ≥ 2 peripheral neuropathy	Substitute CARBOplatin AUC 5 or 50% reduction of CISplatin dose after recovery to grade ≤ 1; 100% dose of etoposide.
Grade 3 (Other than mucositis or alopecia)	Delay until recovery to Grade 1. Then reduce dose of CISplatin and etoposide to 75%.

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

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

PREMEDICATIONS:

Hydration prior and post CISplatin administration (Refer to local policy or see recommendations above).

OTHER SUPPORTIVE CARE: No specific recommendations

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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

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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
3	09/01/2019	Updated CISplatin hydration protocol	Prof Maccon Keane
4	04/09/2019	Reviewed. Update of etoposide renal dosing	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

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