

## CISplatin (75mg/m<sup>2</sup>) + Etoposide (100mg/m<sup>2</sup>) +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 <sup>2</sup>	IV Infusion	1000ml 0.9% NaCl over 1 hour	Every 21 days for 4 cycles
2	1	CISplatin <sup>a</sup>	<sup>b</sup> 75mg/m <sup>2</sup>	IV Infusion	1000ml 0.9% NaCl over 2 hours	Every 21 days for 4 cycles

**<sup>a</sup>Pre and post hydration therapy required for CISplatin**

See local hospital policy recommendations.

Suggested prehydration for CISplatin therapy:

- The administration of etoposide in 1000ml 0.9% NaCl over 1 hour as detailed above may be considered as pre-hydration for CISplatin
- Administer CISplatin as described above

Post hydration:

- Administer 10mmol magnesium sulphate (MgSO<sub>4</sub>) and 20mmol potassium chloride (KCl) in 1000 ml 0.9% NaCl over 2 hours

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)

<sup>b</sup>The total dose of CISplatin may be fractionated and given over 3 days i.e. 25mg/m<sup>2</sup> on day 1

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

NCCP Regimen: CISplatin (75mg/m <sup>2</sup> ) Etoposide (100mg/m <sup>2</sup> ) and Thoracic Radiotherapy-21 day	Published: 10/09/2015 Review: 24/06/2026	Version number: 5
Tumour Group: Lung NCCP Regimen Code: 00279	ISMO Contributor: Prof Maccon Keane	Page 1 of 5

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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
$\geq 1.5$	<b>and</b>	$\geq 100$	100%
1-1.49	<b>or</b>	75-99	75%
$< 1$	<b>or</b>	$< 75$	DELAY

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Tumour Group: Lung NCCP Regimen Code: 00279	ISMO Contributor: Prof Maccon Keane	Page 2 of 5
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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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Tumour Group: Lung NCCP Regimen Code: 00279	ISMO Contributor: Prof Maccon Keane	Page 3 of 5
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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

## 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. Nephrotoxicity Associated with CISplatin EviQ ID: 184 v.3  
<https://www.eviq.org.au/clinical-resources/side-effect-and-toxicity-management/prophylaxis-and-prevention/184-nephrotoxicity-associated-with-CISplatin>
3. Portilla D et al. CISplatin nephrotoxicity. UptoDate Accessed August2019  
<https://www.uptodate.com/contents/cisplatin-nephrotoxicity>
4. 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)
5. Cisplatin Summary of Product Characteristics HPRA. Last updated: 11/03/2019. Accessed June 2021 Available at:  
<https://www.hpra.ie/img/uploaded/swedocuments/Final%20approved%20SPC%20PA0822.199.001.pdf>
6. Etoposide 20 mg/ml Concentrate for Solution for Infusion Summary of Product Characteristics. HPRA Last updated: 17/05/2021 Accessed June 2021 Available at:  
[http://www.hpra.ie/img/uploaded/swedocuments/Licence\\_PA2059-036-001\\_17052021114619.pdf](http://www.hpra.ie/img/uploaded/swedocuments/Licence_PA2059-036-001_17052021114619.pdf)
7. Dosage Adjustment for Cytotoxics in Renal Impairment January 2009; North London Cancer Network.
8. Dosage Adjustment for Cytotoxics in Hepatic Impairment January 2009; North London Cancer Network .

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Tumour Group: Lung NCCP Regimen Code: 00279	ISMO Contributor: Prof Maccon Keane	Page 4 of 5
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9. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V3 2021. Available at: <https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.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
3	09/01/2019	Updated CISplatin hydration protocol	Prof Maccon Keane
4	04/09/2019	Reviewed. Update of etoposide renal dosing	Prof Maccon Keane
5	24/06/2021	Reviewed. Updated CISplatin hydration protocol.	Prof Maccon Keane

Comments and feedback welcome at [oncologydrugs@cancercontrol.ie](mailto:oncologydrugs@cancercontrol.ie).

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Tumour Group: Lung NCCP Regimen Code: 00279	ISMO Contributor: Prof Maccon Keane	Page 5 of 5
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