CARBOplatin and Oral Etoposide Therapy - 21days

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
Small cell lung cancer (SCLC) extensive disease	C34	00319a	N/A

* This applies to post 2012 indications

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.

CARBOplatin is administered on day 1 and etoposide is administered on three consecutive days (Days 1-3) of a 21 day cycle until disease progression or unacceptable toxicity develops.

Facilities to treat anaphylaxis MUST be present when systemic anti-cancer therapy (SACT) is administered.

Day	Drug	Dose	Route and Method of Administration	Diluent & Rate	Cycle
1	CARBOplatin[a]	AUC 5	IV infusion	500mL glucose 5% over 30 minutes	Every 21 days
1-3	Etoposide	100mg/m^2 twice daily[b,c]	PO	N/A	Every 21 days
[a] CARBOplatin is administered prior to etoposide					
[b] The standard oral etoposide dose is approximately twice the effective intravenous etoposide dose i.e.200 mg/m^2 (*orally*) = 100 mg/m^2 (*intravenously*). Prediction of oral dosing based on intravenous dose may be unreliable therefore it is recommended to titrate the oral dose to achieve maximal effect and minimise toxicity.					
[c] Etoposide capsules should be taken on an empty stomach. Etoposide is commonly available as 50mg and 100mg capsules					

Note: Administration volumes and fluids have been standardised to facilitate electronic prescribing system builds

CARBOplatin dose:

The dose in mg of CARBOplatin to be administered is calculated as follows:

Dose (mg) = target AUC (mg/mL x minute) x (GFR mL/minute +25)

- Measured GFR (e.g. nuclear renogram) is preferred whenever feasible
- Estimation of GFR (eGFR) can be done by using the Wright formula to estimate GFR or the Cockcroft and Gault formula to measure creatinine clearance
- The GFR used to calculate the AUC dosing should not exceed 125mL/minute
- For obese patients and those with a low serum creatinine, for example, due to low body weight or post-operative asthenia, estimation using formulae may not give accurate results; measured GFR is recommend
    - where obesity (body mass index [BMI] ≥30kg/m^2) or overweight (BMI 25-29.9) is likely to lead to an overestimate of GFR and isotope GFR is not available the use of the adjusted ideal body weight in the Cockcroft and Gault formula may be considered
    - where serum creatinine is less than 63 micromol/L, the use of a creatinine value of 62 micromol/L or a steady pre-operative creatinine value may be considered
- These comments do not substitute for the clinical judgement of a physician experienced in prescription of CARBOplatin

WRIGHT FORMULA

There are two versions of the formula depending on how serum creatinine values are obtained, by the kinetic Jaffe method or the enzymatic method. The formula can be further adapted if covariant creatine kinase (CK) values are available (not shown).

1. *SCr measured using enzymatic assay*.

$$\text{GFR (mL/minute)} = \frac{(6230 - 32.8 \times \text{Age}) \times \text{BSA} \times (1 - 0.23 \times \text{Sex})}{\text{SCr (micromol/minute)}}$$

2. *SCr measured using Jaffe assay*

$$\text{GFR (mL/minute)} = \frac{(6580 - 38.8 \times \text{Age}) \times \text{BSA} \times (1 - 0.168 \times \text{Sex})}{\text{SCr (micromol/minute)}}$$

Key: Sex = 1 if female, 0 if male; Age in years; BSA= DuBois BSA

COCKCROFT-GAULT FORMULA

$$\text{GFR (ml/min)} = \frac{\text{S} \times (140 - \text{age in years}) \times \text{wt (kg)}}{\text{serum creatinine (micromol/L)}}$$

S= 1.04 for females and 1.23 for males

ELIGIBILITY:

- Indication as above
- Patients unsuitable for treatment with CISplatin based regimens
- ECOG 0-2 (0-3 in patients < 70)

EXCLUSIONS:

- Hypersensitivity to CARBOplatin* etoposide or any of the excipients
- Pregnancy
- Breastfeeding

*If it is felt that the patient may have a major clinical benefit from CARBOplatin, it may in exceptional circumstances be feasible to rechallenge a patient with a prior mild hypersensitivity reaction e.g. using a desensitisation protocol, but only with immunology advice, premedication as advised, and a desensitisation protocol under carefully controlled conditions with resuscitation facilities available and medical and/or ITU/ HDU supervision

PRESCRIPTIVE AUTHORITY:

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

TESTS:

Baseline tests:

- Blood renal and liver profile
- Isotope GFR measurement (preferred) or GFR /CrCl estimation
- Audiology referral as clinical indicated

Regular tests:

- FBC weekly prior to treatment
- Renal and liver profile before 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 in haematological toxicity

ANC ($x10^9$/L)		Platelets ($x10^9$/L)	Dose
≥ 1.0	and	≥ 100	100%
0.5 to <1.0	And/or	75 to < 100	Delay one week until recovery
<0.5 or neutropenic fever	And/or	<50	Delay and consider dose reduction for etoposide and carboplatin by 25%

Renal and Hepatic Impairment:

Table 2: Dose modification of CARBOplatin and etoposide in renal and hepatic impairment

Drug	Renal Impairment		Hepatic Impairment	
CARBOplatin[a]	See note below[b]		No dose modification required	
Etoposide[c]	**CrCl (mL/min)**	**Dose**	**Bilirubin (micromol/L)**	**Dose**
	>50	No dose adjustment is needed	Bilirubin < 50 and normal albumin and normal renal function	No need for dose adjustment is expected
	10-50	75% of the original dose, increase if tolerated.	Bilirubin ≥50 or decreased albumin levels.	Consider 50% of the dose, increase if tolerated.
	Haemodialysis	Not dialysed, consider 75% of the original dose.		
[a] CARBOplatin renal and hepatic –NCCP standardisation [c] Etoposide: Renal and hepatic aligned to Giraud et al 2023 recommendations for etoposide IV as agreed lead clinical reviewer.				

[b]Renal dysfunction and CARBOplatin:

- Patients with CrCl values of <60mL/minute are at greater risk of developing myelosuppression
- If GFR between 20 to ≤ 30mL/minute, CARBOplatin should be administered with extreme caution
- If GFR ≤ 20mL/minute, CARBOplatin should not be administered at all
- If Cockcroft & Gault or Wright formula are used, the dose should be calculated as required per cycle based on a serum creatinine obtained within 48 hours of drug administration

If isotope GFR is used, the dose can remain the same provided the serum creatinine is ≤110% of its value at the time of the isotope measurement. If the serum creatinine increases, consideration should be given to remeasuring the GFR or to estimating it using Cockcroft & Gault or Wright formulae

Table 3: Dose modification schedule based on adverse events

Adverse reactions	Recommended dose modification
Grade ≥ 3 (Other than mucositis or alopecia)	Delay until recovery to Grade 1. Then reduce dose of CARBOplatin and etoposide to 75%

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

- As outlined in the NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting- Available on NCCP website

CARBOplatin: High **(Refer to local policy)**
Etoposide: Minimal to Low **(Refer to local policy)**

For information:
Within NCIS regimens, antiemetics have been standardised by the Medical Oncologists and Haemato-oncologists. Information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for Inclusion in NCIS (Medical Oncology) - Available on the NCCP website
- NCCP Supportive Care Antiemetic Medicines for Inclusion in NCIS (Haemato-oncology) - Available on the NCCP website

PREMEDICATIONS: Not usually required unless patient has experienced a previous hypersensitivity

OTHER SUPPORTIVE CARE: No specific recommendations

ADVERSE EFFECTS

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details

REGIMEN SPECIFIC COMPLICATIONS

- **Neurotoxicity and ototoxicity:** Neurological evaluation and an assessment of hearing should be performed on a regular basis, especially in patients receiving high dose CARBOplatin. Neurotoxicity, such as parasthesia, decreased deep tendon reflexes, and ototoxicity are more likely seen in patients previously treated with CISplatin, other platinum treatments and other ototoxic agents. Frequency of neurologic toxicity is also increased in patients older than 65 years.

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for information.

REFERENCES:

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2. Rossi, A., M. Di Maio, P. Chiodini, et al. Carboplatin- or cisplatin-based chemotherapy in first-line treatment of small-cell lung cancer: the COCIS meta-analysis of individual patient data. J Clin Oncol 2012; 30(14):1692-1698
3. Ekhart C, Rodenhuis S et al. Carboplatin dosing in overweight and obese patients with normal renal function, does weight matter? Cancer Chemother Pharmacol 2009; 64:115-122.
4. Appropriate chemotherapy dosing for obese adult patients with cancer: American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol 2012; 30 (13) 1553-1561.
5. NCCN CARBOplatin dosing in adults https://www.nccn.org/docs/default-source/clinical/ordertemplates/appendix_b.pdf?sfvrsn=6286822e_6
6. Wright JG, Boddy AV, et al, Estimation of glomerular filtration rate in cancer patients. British Journal of Cancer 2001; 84(4):452-459
7. NCCP Classification Document for Systemic AntiCancer Therapy (SACT) Induced Nausea and Vomiting.V6 2025 Available at : https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classificationdocument-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf
8. CARBOplatin Summary of Product Characteristics Last updated 04/09/2024 Accessed April 2025. Available from NCCP upon request

9. Etoposide Summary of Product Characteristics. Last updated: 27/02/2024. Accessed April 2025. Available from NCCP upon request

Version	Date	Amendment	Approved By
1	03/05/2016		Dr Maccon Keane
2	02/05/2018	Updated with new NCCP regimen template. Updated title, dosing in renal impairment and emetogenic status.	Prof Maccon Keane
3	13/05/2020	Reviewed. Update of emetogenic potential.	Prof Maccon Keane
4	30/08/2022	Update of CARBOplatin infusion time.Updated standard wording for CARBOplatin dosing and creatinine value. Updated baseline tests. Updated dose modifications for haematological toxicity.	Prof Maccon Keane
5	12/09/2025	Regimen reviewed.Updated exclusion criteria. Updated baseline testing.Updated Table 1 dose modification in haematological toxicity. Updated renal and hepatic dose modifications to align with Giraud et al 2023 for etoposide. Updated regimen in line with NCCP standardisation.	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.