CARBOplatin (AUC4-6) Monotherapy-28 days

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved Reimbursement Status*
First line adjuvant therapy of • ovarian carcinoma of epithelial origin • primary peritoneal carcinoma • fallopian tube cancer where combination therapy is not suitable.	 C56 C48 C57	 00251a 00251b 00251c	N/A
First line therapy of advanced Stage 3 and 4 • ovarian carcinoma of epithelial origin • primary peritoneal carcinoma • fallopian tube cancer where surgery is not feasible and where combination therapy is not suitable.	 C56 C48 C57	 00251d 00251e 00251f	N/A
Treatment of recurrent, platinum-sensitive, • invasive ovarian carcinoma of epithelial origin • primary peritoneal carcinoma • fallopian tube cancer	 C56 C48 C57	 00251g 00251h 00251i	N/A
Metastatic breast carcinoma[i]	C50	00251j	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 once every **28 days** until disease progression or unacceptable toxicity develops.

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

Drug	Dose	Route	Diluent & Rate	Cycle
CARBOplatin	AUC (4-6)	IV infusion	500mL glucose 5% over 30 minutes	Every 28 days

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

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibly of the prescribing clinician. and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPSACTregimens

CARBOplatin dose:

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

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

- **Measured GFR** (e.g. nuclear renogram) is preferred whenever feasible.
- **Estimation of GFR** (eGFR) can be done by using the Wright formula or using the Cockcroft and Gault formula to measure creatinine clearance.
- The GFR used to calculate the AUC dosing should not exceed 125mL/min.
- For obese patients and those with a low serum creatinine, for example, due to low body weight or post-operative asthenia, the formulae may not give accurate results and measured GFR is recommended.
  - Where obesity (body mass index [BMI] ≥ 30 kg/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 for Cockcroft and Gault 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.*

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

2. *SCr measured using Jaffe assay*

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

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

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibly of the prescribing clinician. and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPSACTregimens

COCKCROFT-GAULT FORMULA

GFR (mL/min) = S x (140 - age in years) x wt (kg)
serum creatinine (micromol/L)

S= 1.04 for females and 1.23 for males

ELIGIBILITY:

- Indications as above
- ECOG status 0-2
- ECOG 0-3 where PS 3 is due to advanced ovarian, primary peritoneal or fallopian tube cancer

EXCLUSIONS:

- Hypersensitivity to CARBOplatin or any of the excipients*.
- Disease progression while receiving platinum based chemotherapy
- Pregnancy or lactation

*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 (1).

PRESCRIPTIVE AUTHORITY:

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

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Isotope GFR measurement (preferred) or GFR / creatinine clearance estimation

Regular tests:

- FBC at day 13-15 and day 21 for first cycles to determine nadir, subsequently before each cycle.
- 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.

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibly of the prescribing clinician. and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPSACTregimens

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant.

Haematological:

Table 1: Dose modification of CARBOplatin in haematological toxicity

ANC ($x10^9$/L)		Platelets ($x10^9$/L)	Dose
≥1	**And**	≥100	100%
<1	**And/or**	<100	Delay one week or until recovery

For some patients especially ECOG 2 or 3, treatment thresholds may be higher.

Renal and Hepatic Impairment:

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

Renal Impairment	Hepatic Impairment
See note below[a]	No dose modification required

[a]Renal dysfunction and CARBOplatin:

- Patients with creatinine clearance values of <60mL/min are at greater risk of developing myelosuppression.
- If GFR between 20 to ≤ 30mL/min, CARBOplatin should be administered with extreme caution
- If GFR ≤ 20mL/min, 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 hrs 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.

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL

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

CARBOplatin: High **(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

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibly of the prescribing clinician. and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPSACTregimens

PREMEDICATIONS: Not usually required

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.
- **Hypersensitivity:** Reactions to CARBOplatin may develop in patients who have been previously exposed to platinum therapy. However allergic reactions have been observed upon initial exposure to CARBOplatin.
- **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:

- Avoid concurrent use with nephrotoxic drugs (e.g. aminoglycosides, furosemide, NSAIDS) due to additive nephrotoxicity. If necessary monitor renal function closely.
- Avoid concurrent use with ototoxic drugs (e.g. aminoglycosides, furosemide, NSAIDS). If necessary perform regular audiometric testing.
- Current drug interaction databases should be consulted for more information.

REFERENCES:

1. NCCN guidelines version 1 2021. Ovarian cancer including fallopian tube cancer and primary peritoneal cancer.
2. Pfisterer J, Plante M, Vergote I. et al. Gemcitabine plus carboplatin compared with carboplatin in patients with platinum-sensitive recurrent ovarian cancer: an intergroup trial of the AGO-OVAR, the NCIC CTG, and the EORTC GCG. J Clin Oncol 2006; 24 (29):4699-4707.
3. ICON3. Paclitaxel plus carboplatin versus standard chemotherapy with either single-agent carboplatin or cyclophosphamide, doxorubicin, and cisplatin in women with ovarian cancer: the ICON3 randomised trial. Lancet 2002; 360(9332): 505-15.
4. ICON2: randomised trial of single-agent carboplatin against three-drug combination of CAP (cyclophosphamide, doxorubicin, and cisplatin) in women with ovarian cancer. ICON Collaborators. International Collaborative Ovarian Neoplasm Study. Lancet 1998; 352(9140): 1571-1576.
5. Decatris MP, Sundar S, O'Byrne KJ. Platinum-based chemotherapy in metastatic breast cancer: current status. Cancer Treat Rev. 2004; 30:53–81.
6. 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.
7. 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.

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibly of the prescribing clinician. and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPSACTregimens

8. NCCN CARBOplatin dosing in adults https://www.nccn.org/docs/default-source/clinical/order-templates/appendix_b.pdf?sfvrsn=6286822e_6
9. Wright JG, Boddy AV, et al, Estimation of glomerular filtration rate in cancer patients. British Journal of Cancer 2001; 84(4):452-459
10. Krens S D, Lassche,Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. Lancet Onco/2019; 20:e201-08. https://doi.org/10.1016/S1470-2045(19)30145-7
11. Dosage Adjustment for Cytotoxics in Renal Impairment January 2009; North London Cancer Network.
12. Dosage Adjustment for Cytotoxics in Hepatic Impairment January 2009; North London Cancer Network.
13. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V4 2022. 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
14. CARBOplatin Summary of Product Characteristics HPRA. Accessed 23/07/2021. Available at: https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA2059-032-001_10112019092721.pdf

From 20/05/2026, this regimen will be reviewed on an 'As Required' basis. Please refer to the version control box for information, and the footer for date of last review. If you wish to suggest any updates to this regimen, please contact oncologydrugs@cancercontrol.ie

Version	Date	Amendment	Approved By
1	10/9/2015		Dr Maccon Keane Dr Dearbhaile O'Donnell
2	27/09/2017	Updated with new NCCP regimen template. Title amended to include dose. Emetogenic status amended from moderate to moderate-high	Prof Maccon Keane
3	04/09/2019	Standardisation of treatment table. Emetogenic potential updated.	Prof Maccon Keane
4	28/07/2021	Reviewed. Updated Carboplatin Dose wording. Updated Baseline tests and dose modification in renal impairment.	Prof Maccon Keane
5	27/07/2022	Updated CARBOplatin infusion time. Updated CARBOplatin dose wording.Updated dose modification of CARBOplatin in haematological toxicity.	Prof Maccon Keane
6	12/06/2026	Update to eligibility section. Amendment to review schedule. Addition of links in emetogenic potential section.	NCCP

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibly of the prescribing clinician. and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPSACTregimens

[i] This regimen is outside its licensed indication in Ireland. Patients should be informed of the unlicensed nature of this indication and consented to treatment in line with the hospital's policy on the use of unlicensed medication and unlicensed or "off label" indications. Prescribers should be aware of their responsibility in communicating any relevant information to the patient and also in ensuring that the unlicensed or "off label" indication has been acknowledged by the hospital's Drugs and Therapeutics Committee, or equivalent, in line with hospital policy.

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibly of the prescribing clinician. and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer

This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPSACTregimens