

## CARBOplatin (AUC4-6) Monotherapy-28 days

### INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
First line adjuvant therapy of <ul style="list-style-type: none"> <li>ovarian carcinoma of epithelial origin</li> <li>primary peritoneal carcinoma</li> <li>fallopian tube cancer</li> </ul> where combination therapy is not suitable.	C56 C48 C57	00251a 00251b 00251c	Hospital
First line therapy of advanced Stage 3 and 4 <ul style="list-style-type: none"> <li>ovarian carcinoma of epithelial origin</li> <li>primary peritoneal carcinoma</li> <li>fallopian tube cancer</li> </ul> where surgery is not feasible and where combination therapy is not suitable.	C56 C48 C57	00251d 00251e 00251f	Hospital
Treatment of recurrent, platinum-sensitive, <ul style="list-style-type: none"> <li>invasive ovarian carcinoma of epithelial origin</li> <li>primary peritoneal carcinoma</li> <li>fallopian tube cancer</li> </ul>	C56 C48 C57	00251g 00251h 00251i	Hospital
Metastatic breast carcinoma <sup>i</sup>	C50	00251j	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.

CARBOplatin is administered once every **28 days** until disease progression or unacceptable toxicity develops.

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

NCCP Regimen: CARBOplatin (AUC 4-6) Monotherapy- 28 day	Published: 10/09/2015 Review: 28/07/2026	Version number: 5
Tumour Group: Gynaecology/Breast NCCP Regimen Code: 00251	ISMO Contributors: Prof Maccon Keane Dr Dearbhaile O'Donnell	Page 1 of 6
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## CARBOplatin dose:

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

$$\text{Dose (mg)} = \text{target AUC (mg/ml x min)} \times (\text{GFR ml/min} + 25)$$

- **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]  $\geq 30 \text{ kg/m}^2$ ) 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*

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

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

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Tumour Group: Gynaecology/Breast NCCP Regimen Code: 00251	ISMO Contributors: Prof Maccon Keane Dr Dearbhaile O'Donnell	Page 2 of 6
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## COCKCROFT-GAULT FORMULA

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

S= 1.04 for females and 1.23 for males

## ELIGIBILITY:

- Indications as above
- Life expectancy >3 months
- 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.

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Tumour Group: Gynaecology/Breast NCCP Regimen Code: 00251	ISMO Contributors: Prof Maccon Keane Dr Dearbhaile O'Donnell	Page 3 of 6
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## DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant.

## Haematological:

**Table 1: Dose modification of CARBOplatin in haematological toxicity**

ANC (x10 <sup>9</sup> /L)		Platelets (x10 <sup>9</sup> /L)	Dose
≥1	<b>And</b>	≥100	100%
<1	<b>and/or</b>	<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
<ul style="list-style-type: none"> <li>Patients with creatinine clearance values of &lt;60ml/min are at greater risk to develop myelosuppression.</li> <li>If GFR between 20 to ≤ 30ml/min, CARBOplatin should be administered with extreme caution.</li> <li>In case of GFR ≤ 20ml/min, carboplatin should not be administered at all.</li> <li>If Cockcroft &amp; 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 should remain the same provided the serum creatinine is ≤ 110% of its value at the time of the isotope measurement. If the serum creatinine is higher than this, consideration should be given to remeasuring the GFR or to recalculating using Cockcroft &amp; Gault or Wright formulae taking care this does result in a dose reduction.</li> </ul>	No dose modification required

## SUPPORTIVE CARE:

**EMETOGENIC POTENTIAL:** High (Refer to local policy).

**PREMEDICATIONS:** Not usually required

**OTHER SUPPORTIVE CARE:** No specific recommendations

NCCP Regimen: CARBOplatin (AUC 4-6) Monotherapy- 28 day	Published: 10/09/2015 Review: 28/07/2026	Version number: 5
Tumour Group: Gynaecology/Breast NCCP Regimen Code: 00251	ISMO Contributors: Prof Maccon Keane Dr Dearbhaile O'Donnell	Page 4 of 6
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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.
- **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.

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NCCP Regimen: CARBOplatin (AUC 4-6) Monotherapy- 28 day	Published: 10/09/2015 Review: 28/07/2026	Version number: 5
Tumour Group: Gynaecology/Breast NCCP Regimen Code: 00251	ISMO Contributors: Prof Maccon Keane Dr Dearbhaile O'Donnell	Page 5 of 6
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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

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

<sup>i</sup> 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.

NCCP Regimen: CARBOplatin (AUC 4-6) Monotherapy- 28 day	Published: 10/09/2015 Review: 28/07/2026	Version number: 5
Tumour Group: Gynaecology/Breast NCCP Regimen Code: 00251	ISMO Contributors: Prof Maccon Keane Dr Dearbhaile O'Donnell	Page 6 of 6
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