CARBOplatin (AUC4-6) Monotherapy-21 days

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	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	00261a 00261b 00261c	Hospital
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	00261d 00261e 00261f	Hospital
Treatment of recurrent, platinum-sensitive, • invasive ovarian carcinoma of epithelial origin • primary peritoneal carcinoma • fallopian tube cancer	C56 C48 C57	00261g 00261h 00261i	Hospital
Metastatic breast carcinoma[i]	C50	00261j	Hospital
Chemoradiation treatment for locally advanced (stage III to IV) squamous cell carcinoma (SCC) of the head and neck, where treatment with CISplatin is not appropriate (AUC 5)	C76	00261k	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.

Gynaecology/breast cancer indications:
CARBOplatin is administered once every **21 days** until disease progression or unacceptable toxicity develops.

Head and neck indication:
CARBOplatin is administered once every **21 days** with concurrent radiotherapy for 3 cycles

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)[a]	IV infusion	500ml glucose 5% over 30 mins	Every 21 days
[a]AUC 5 is the recommended dose for head and neck cancer				

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) may be performed using the Wright formula to estimate GFR or the Cockcroft and Gault formula to estimate 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, estimation using formulae may not give accurate results; 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

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
- 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.

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, 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 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: High **(Refer to local policy).**

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). Consider audiometric testing.
- Current drug interaction databases should be consulted for more information.

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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 to high	Prof Maccon Keane
3	04/09/2019	Treatment table standardised. Emetogenic potential updated.	Prof Maccon Keane
4	28/07/2021	Reviewed. Updated Carboplatin Dose wording. Added to 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	26/04/2023	Addition of HNSCC indication. Update to eligibility, testing, renal impairment and interactions sections.	Dr Cliona Grant

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

[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.