CARBOplatin (AUC4-6) Monotherapy-28 days

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	*Reimbursement Indicator
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	
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	
Treatment of recurrent, platinum-sensitive, • invasive ovarian carcinoma of epithelial origin • primary peritoneal carcinoma • fallopian tube cancer	C56 C48 C57	00251g 00251h 00251i	
Metastatic breast carcinoma[ii].	C50	00251j	

**If a reimbursement indicator (e.g. ODMS, CDS[i]) is not defined, the drug and its detailed indication have not gone through the formal reimbursement process as legislated for in the Health (Pricing and Supply of Medical Goods) Act 2013.*

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 and Method of Administration	Diluent & Rate	Cycle
CARBOplatin	AUC (4-6)	IV infusion	250-500ml glucose 5% (or 0.9% NaCl) over 60 min	Every 28 days

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 Cockroft and Gault formula to measure creatinine clearance

- The GFR used to calculate the AUC dosing should not exceed 125ml/min.
- For obese and anorexic patients the formulae may not give accurate results and measured GFR is recommended. Where obesity or overweight is likely to lead to an overestimate of GFR and isotope GFR is not available the use of the adjusted ideal body weight for Cockroft and Gault may be considered (2).

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*.

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

2. *SCr measured using Jaffe assay*

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

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

ELIGIBILTY:

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

- Blood renal and liver profile

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.

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**	< 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
• Patients with creatinine clearance values of < 60ml/min are at greater risk to develop myelosuppression. • In case of GFR ≤ 20ml/min carboplatin should not be administered at all. • If Cockroft & Gault or Wright formula are used, the dose should be adjusted 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 Cockroft & Gault or Wright formulae taking care this does result in a dose reduction	Probably no dose modification required

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Moderate-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). If necessary perform regular audiometric testing.
- Current drug interaction databases should be consulted for more information.

ATC CODE:

CARBOplatin - L01XA02

REFERENCES:

1. NCCN Guidelines Version3.2017 Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer
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3. Wright JG, Boddy AV, et al, Estimation of glomerular filtration rate in cancer patients. British Journal of Cancer 2001; 84(4):452-459
4. 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.
5. 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.
6. 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.
7. Decatris MP, Sundar S, O'Byrne KJ. Platinum-based chemotherapy in metastatic breast cancer: current status. Cancer Treat Rev. 2004;30:53–81.
8. 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.
9. NCCN Clinical Practice Guidelines in Oncology: Antiemesis Version2. 2017 March 28, 2017
10. Carboplatin Summary of Product Characteristics Accessed September 2017. Available at http://www.hpra.ie/img/uploaded/swedocuments/LicenseSPC_PA0749-004-001_19062014145041.pdf

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

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

[i] ODMS – Oncology Drug Management System

CDS – Community Drug Schemes (CDS) including the High Tech arrangements of the PCRS community drug schemes
Further details on the Cancer Drug Management Programme is available at;
http://www.hse.ie/eng/services/list/5/cancer/profinfo/medonc/cdmp/

[ii] This indication is outside the licensed indications for CARBOplatin 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.