CARBOplatin (AUC4-6) Monotherapy-28 days

INDICATIONS FOR USE:

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>ICD10 Code</th>
<th>Regimen Code</th>
<th>*Reimbursement Indicator</th>
</tr>
</thead>
<tbody>
<tr>
<td>First line adjuvant therapy of ovarian carcinoma of epithelial origin</td>
<td>C56</td>
<td>00251a</td>
<td></td>
</tr>
<tr>
<td>First line adjuvant therapy of primary peritoneal carcinoma</td>
<td>C48</td>
<td>00251b</td>
<td></td>
</tr>
<tr>
<td>First line adjuvant therapy of fallopian tube cancer</td>
<td>C57</td>
<td>00251c</td>
<td></td>
</tr>
<tr>
<td>First line therapy of advanced Stage 3 and 4 ovarian carcinoma of epithelial origin</td>
<td>C56</td>
<td>00251d</td>
<td></td>
</tr>
<tr>
<td>First line therapy of advanced Stage 3 and 4 primary peritoneal carcinoma</td>
<td>C48</td>
<td>00251e</td>
<td></td>
</tr>
<tr>
<td>First line therapy of advanced Stage 3 and 4 fallopian tube cancer</td>
<td>C57</td>
<td>00251f</td>
<td></td>
</tr>
<tr>
<td>Treatment of recurrent, platinum-sensitive, invasive ovarian carcinoma of epithelial origin</td>
<td>C56</td>
<td>00251g</td>
<td></td>
</tr>
<tr>
<td>Treatment of recurrent, platinum-sensitive, primary peritoneal carcinoma</td>
<td>C48</td>
<td>00251h</td>
<td></td>
</tr>
<tr>
<td>Treatment of recurrent, platinum-sensitive, fallopian tube cancer</td>
<td>C57</td>
<td>00251i</td>
<td></td>
</tr>
<tr>
<td>Metastatic breast carcinoma</td>
<td>C50</td>
<td>00251j</td>
<td></td>
</tr>
</tbody>
</table>

*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 patient's individual clinical circumstances.

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route and Method of Administration</th>
<th>Diluent &amp; Rate</th>
<th>Cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>CARBOplatin</td>
<td>AUC (4-6)</td>
<td>IV infusion</td>
<td>250-500ml glucose 5% (or 0.9% NaCl) over 60 min</td>
<td>Every 28 days</td>
</tr>
</tbody>
</table>

**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 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.*

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

2. *Scr measured using Jaffe assay*

\[
GFR \text{ (ml/min)} = \frac{(6580 - 38.8 \times \text{Age}) \times \text{BSA}}{\text{Scr (μmol/min)}} (1 - 0.168 \times \text{Sex})
\]

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

**COCKCROFT-GAULT FORMULA**

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

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

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/NCCPchemoregimens
*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**

<table>
<thead>
<tr>
<th>ANC (x10⁹ /L)</th>
<th>Platelets (x10⁹ /L)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 1 and</td>
<td>&gt; 100</td>
<td>100%</td>
</tr>
<tr>
<td>&lt; 1 and</td>
<td>&lt; 100</td>
<td>Delay one week or until recovery</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Renal Impairment</th>
<th>Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Patients with creatinine clearance values of &lt; 60ml/min are at higher risk to</td>
<td>Probably no dose modification required</td>
</tr>
<tr>
<td>develop myelosuppression.</td>
<td></td>
</tr>
<tr>
<td>• In case of GFR ≤ 20ml/min carboplatin should not be administered at all.</td>
<td></td>
</tr>
<tr>
<td>• If Cockroft &amp; Gault or Wright formula are used, the dose should be adjusted</td>
<td></td>
</tr>
<tr>
<td>per cycle based on a serum creatinine obtained within 48 hrs of drug administration.</td>
<td></td>
</tr>
<tr>
<td>• If isotope GFR is used, the dose should remain the same provided the serum</td>
<td></td>
</tr>
<tr>
<td>creatinine is ≤110% of its value at the time of the isotope measurement. If the</td>
<td></td>
</tr>
<tr>
<td>serum creatinine is higher than this, consideration should be given to</td>
<td></td>
</tr>
<tr>
<td>remeasuring the GFR or to recalculating using Cockroft &amp; Gault or Wright</td>
<td></td>
</tr>
<tr>
<td>formulae taking care this does result in a dose reduction.</td>
<td></td>
</tr>
</tbody>
</table>

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.
NCCP Chemotherapy Regimen

ATC CODE:
CARBOplatin - L01XA02

REFERENCES:
1. NCCN Guidelines Version3.2017 Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer

<table>
<thead>
<tr>
<th>Version</th>
<th>Date</th>
<th>Amendment</th>
<th>Approved By</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10/9/2015</td>
<td></td>
<td>Dr Maccon Keane</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Dr Dearbhaile O’Donnell</td>
</tr>
<tr>
<td>2</td>
<td>27/09/2017</td>
<td>Updated with new NCCP regimen template. Title amended to include dose. Emetogenic status amended from moderate to moderate-high</td>
<td>Prof Maccon Keane</td>
</tr>
</tbody>
</table>

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

1 ODMS – Oncology Drug Management System

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NCCP Chemotherapy Regimen

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/proinfo/medonc/cdmp/

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.