Carboplatin Monotherapy-21 days

**INDICATIONS FOR USE:**

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>ICD10</th>
<th>Protocol Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>First line adjuvant therapy of ovarian carcinoma of epithelial origin</td>
<td>C56</td>
<td>00261a</td>
</tr>
<tr>
<td>primary peritoneal carcinoma</td>
<td>C48</td>
<td>00261b</td>
</tr>
<tr>
<td>fallopian tube cancer</td>
<td>C57</td>
<td>00261c</td>
</tr>
<tr>
<td>where combination therapy is not suitable.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First line therapy of advanced Stage 3 and 4</td>
<td>C56</td>
<td>00261d</td>
</tr>
<tr>
<td>ovarian carcinoma of epithelial origin</td>
<td>C48</td>
<td>00261e</td>
</tr>
<tr>
<td>primary peritoneal carcinoma</td>
<td>C57</td>
<td>00261f</td>
</tr>
<tr>
<td>fallopian tube cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>where surgery is not feasible and where combination therapy is not suitable.</td>
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<td></td>
</tr>
<tr>
<td>Treatment of recurrent, platinum-sensitive, invasive ovarian carcinoma of</td>
<td>C56</td>
<td>00261g</td>
</tr>
<tr>
<td>epithelial origin</td>
<td>C48</td>
<td>00261h</td>
</tr>
<tr>
<td>primary peritoneal carcinoma</td>
<td>C57</td>
<td>00261i</td>
</tr>
<tr>
<td>fallopian tube cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metastatic breast carcinoma.</td>
<td>C50</td>
<td>00261j</td>
</tr>
</tbody>
</table>

**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

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*This information is valid only on the day of printing, for any updates please check [www.hse.ie/NCCPchemoprotocols](http://www.hse.ie/NCCPchemoprotocols)
*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).

**TESTS:**

*Baseline tests*: FBC, U&E, LFT, creatinine

*Regular tests*: FBC at day 13-15 and day 21 for first cycles to determine nadir, subsequently before each cycle.
U&E, LFT creatinine, before each cycle

**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 21 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>1</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 Cockcroft 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.*

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

2. *SCr measured using Jaffe assay*

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

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
DOSE MODIFICATIONS:
- Any dose modification should be discussed with a Consultant

Haematological:

On Treatment Day

<table>
<thead>
<tr>
<th>ANC (x 10^9/L)</th>
<th>Platelets (x 10^9/L)</th>
<th>Dose Carboplatin</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1 and ≥ 100</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>≤ 1 and &lt; 100</td>
<td>Delay one week or until recovery</td>
<td></td>
</tr>
</tbody>
</table>

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

Renal dysfunction:
- Patients with creatinine clearance values of less than 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

- Hepatic dysfunction: No dose modification required.

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Moderate (Refer to local policy)

PREMEDICATIONS: None usually required.

TAKE HOME MEDICATIONS: None 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). When necessary perform regular audiometric testing
- Carboplatin may interact with aluminium to form a black precipitate. Needles, syringes, catheters or IV administration sets that contain aluminium parts which may come into contact with carboplatin, should not be used for the preparation or administration of the drug.
- Current drug interaction databases should be consulted for more information.

**ATC CODE:**
Carboplatin - L01XA02

**REIMBURSEMENT CATEGORY:**
Carboplatin is funded through local hospital budgets (Nov. 2014).
REFERENCES:

1. NCCN Guidelines Version1.2015 Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer
Comments and feedback welcome at oncologydrugs@cancercontrol.ie

1 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.