CARBOplatin (AUC1.5) Chemoradiation Therapy-7 days

INDICATIONS FOR USE:

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>ICD10</th>
<th>Regimen Code</th>
<th>*Reimbursement Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemoradiation commencing 3 to 8 weeks after the completion of induction</td>
<td></td>
<td>00332a</td>
<td>Hospital</td>
</tr>
<tr>
<td>chemotherapy with TPF in patients with Stage III or IV locally advanced</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>squamous cell carcinoma (SCC) of the head and neck¹</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹If the reimbursement status is not defined, the indication has yet to be assessed through the formal HSE reimbursement process.

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 7 days concomitantly with radiotherapy for 7 weeks to start 3 to 8 weeks (day 22 to day 56) following start of third cycle of induction chemotherapy (Reference NCCP Regimen 00315 Neoadjuvant DOCEtaxel, CISplatin, 5-Fluorouracil and Chemoradiation and Surgery or NCCP Regimen 00323 DOCEtaxel, CISplatin and 5-Fluorouracil Chemoradiation Therapy for details of induction chemotherapy).

CARBOplatin is only to be administered concurrently with radiotherapy. Treatment with CARBOplatin should be discontinued if radiotherapy is truncated.

<table>
<thead>
<tr>
<th>Day</th>
<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>1</td>
<td>CARBOplatin</td>
<td>AUC (1.5)</td>
<td>IV infusion</td>
<td>500ml glucose 5% over 60 min</td>
<td>Repeat every 7 days for a total of 7 cycles</td>
</tr>
</tbody>
</table>

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 (4).

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NCCP Chemotherapy Regimen

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

COCKCROFT-GAULT FORMULA

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

\[
\text{serum creatinine (micromol/L)}
\]

\[
S = 1.04 \text{ for females and 1.23 for males}
\]

ELIGIBILITY:

- Indications as above
- ECOG status 0-2

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 (3).

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist

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NCCP Regimen: CARBOplatin (AUC 1.5) Chemoradiation Therapy- 7days

Published: 20/06/2016
Review: 20/06/2020

Version number: 2

Tumour Group: Head & Neck
NCCP Regimen Code: 00332

ISM0 Contributors:
Prof Maccon Keane

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TESTS:

Baseline tests:
- Blood renal and liver profile

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

<table>
<thead>
<tr>
<th>ANC (x10^9/L)</th>
<th>Platelets (x10^9/L)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 1 and &gt; 100</td>
<td>&gt; 100</td>
<td>100%</td>
</tr>
<tr>
<td>&lt; 1 and &lt; 100</td>
<td></td>
<td>Delay one week or until recovery</td>
</tr>
</tbody>
</table>

For some patients especially ECOG 2, 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 greater 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 per</td>
<td></td>
</tr>
<tr>
<td>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 remeasuring</td>
<td></td>
</tr>
<tr>
<td>the GFR or to recalculating using Cockroft &amp; Gault or Wright formulae taking</td>
<td></td>
</tr>
<tr>
<td>care this does result in a dose reduction.</td>
<td></td>
</tr>
</tbody>
</table>

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Moderate (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 paraesthesia, 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:
3. NCCN Guidelines Version3.2017 Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer

**Version** | **Date** | **Amendment** | **Approved By**
--- | --- | --- | ---
1 | 20/06/2016 |  | Dr Maccon Keane
2 | 20/06/2018 | Applied new NCCP regimen template, standardization of treatment table | Prof Maccon Keane

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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.

2 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/proinfo/medonc/cdmp/