CARBOplatin (AUC1.5) Chemoradiation Therapy-7 days

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Chemoradiation commencing 3 to 8 weeks after the completion of induction chemotherapy with TPF in patients with Stage III or IV locally advanced squamous cell carcinoma (SCC) of the head and neck[i]	C76	00332a	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.

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.

Day	Drug	Dose	Route and Method of Administration	Diluent & Rate	Cycle
1	CARBOplatin	AUC (1.5)	IV infusion	250ml glucose 5% over 30 min	Repeat every 7 days for a total of 7 cycles

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 Cockcroft and Gault formula to measure 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.

o 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 in the Cockcroft and Gault formula may be considered.
o 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

EXCLUSIONS:

- Hypersensitivity to CARBOplatin or any of the excipients
- Disease progression while receiving platinum based chemotherapy
- Pregnancy or lactation

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist

TESTS:

Baseline tests:

- Blood renal and liver profile
- Isotope GFR measurement (preferred) or GFR / Cr 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, 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 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 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 Cockcroft & Gault or Wright formulae taking care this does result in a dose reduction	Probably no dose modification required

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

CARBOplatin 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 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.

REFERENCES:

1. Posner MR, Hershock DM et al. Cisplatin and Fluorouracil Alone or with Docetaxel in Head and Neck Cancer. NEJM 2007; 357:1705-15
2. Haddad R, O'Neill A et al. Induction chemotherapy followed by concurrent chemoradiotherapy (sequential chemoradiotherapy) versus concurrent chemoradiotherapy alone in locally advanced head and neck cancer (PARADIGM): a randomised phase 3 trial. Lancet Oncol 2013; 14 (3):257-264.
3. 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.
4. Wright JG , Boddy AV et al, Estimation of glomerular filtration rate in cancer patients. British Journal of Cancer 2001; 84(4);452-459
5. Ekhart C, Rodenhuis S et al. CARBOplatin dosing in overweigt and obese patients with normal renal function , does weight matter? Cancer Chemother Pharmacol 2009 64:115-122
6. NCCN CARBoplatin dosing in adults https://www.nccn.org/docs/default-source/clinical/order-templates/appendix_b.pdf?sfvrsn=6286822e_6
7. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V4 2022. Available at https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf:
8. CARBOplatin Summary of Product Characteristics Accessed August 2022 Available at https://www.hpra.ie/img/uploaded/swedocuments/LicenseSPC_PA0437-017-002A_25062018161037.pdf

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
3	15/07/2020	Standardisation of treatment table Exclusion criteria Updated references	Prof Maccon Keane
4	27/08/2022	Updated CARBOplatin infusion time. Updated standard wording for CARBOplatin dosing and creatinine value. Updated baseline tests. Updated Dose modification of CARBOplatin in haematological toxicity	Prof Maccon Keane

		Updated emetogenic potential.. Removed ATC codes.	

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

[i] 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.