Carboplatin and radiotherapy

Indication
Chemo-radiation for head and neck cancers when cisplatin or cetuximab are contraindicated.

Performance status 0-1

ICD-10 codes
Codes prefixed with C00-C13

Regimen details

Day	Drug	Dose	Route
1	Carboplatin	AUC 2*	IV infusion

* Carboplatin dose calculated using the Calvert equation: **Carboplatin dose (mg) = AUC (CrCl +25)**
The creatinine clearance (CrCl) is calculated using the Cockcroft and Gault equation. However, for patients where the creatinine level may not truly reflect renal function (e.g. in extremes of BSA or debilitated patients) an EDTA should be performed. CrCl should be capped at 125mL/min.

Cycle frequency
7 days

Number of cycles
Maximum of 6-7 cycles

Administration
Carboplatin is administered in 250-500mL glucose 5% over 30-60 minutes.

Patients should be observed closely for hypersensitivity reactions, particularly during the first and second infusions. Hypersensitivity reactions may occur within a few minutes following the initiation of the infusion of carboplatin. Facilities for the treatment of hypotension and bronchospasm **must** be available.

If hypersensitivity reactions occur, minor symptoms such as flushing or localised cutaneous reactions do not require discontinuation of therapy. The infusion may be temporarily interrupted and when symptoms improve restarted at a slower infusion rate. Chlorphenamine 10mg IV may be administered. Severe reactions, such as hypotension, bronchospasm or generalised rash/erythema require immediate discontinuation of carboplatin and appropriate therapy.

Pre-medication
None usually required.

Emetogenicity
This regimen has a moderate emetogenic potential

Additional supportive medication
Mouthwashes as per local policy.
Antiemetics as per local policy.
Loperamide if required.

Extravasation

Carboplatin is an irritant (Group 3)

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days
Magnesium	14 days

Baseline EDTA if suspected or significant renal dysfunction.

Investigations - pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	72 hours
U+E (including creatinine)	72 hours
LFTs	72 hours
Magnesium	72 hours

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Investigation	**Limit**
Neutrophils	≥ 1.0 x 10^9/L
Platelets	≥ 100 x 10^9/L
Creatinine Clearance (CrCl)	> 30mL/min (and <10% change in CrCl from previous cycle)
Bilirubin	≤ 3 x ULN
AST/ALT	≤ 5 x ULN

Dose modifications

- **Haematological toxicity**

If neutrophils < 1.0 x 10^9/L and/or platelets ≤ 100 x 10^9/L delay 1 week or until recovery.

- **Renal impairment**

CrCl (mL/min)	**Carboplatin dose**
> 30	100%
20-30	Consider if time allows EDTA then 100% dose
< 20	Omit

If CrCl falls by more than 10% from the previous cycle then consider recalculating the dose.

- **Hepatic impairment**

Transient increases in liver enzymes have been seen in patients being treated with carboplatin although no dose reduction is usually required. If bilirubin ≥ 3 x ULN and/or transaminases ≥ 5 x ULN discuss with consultant.

- **Other toxicities**

For peripheral neuropathy ≥ grade 3 discuss with consultant.
For all other grade 3-4 toxicities (except alopecia) delay treatment until resolved to ≤ grade 1. If delays of > 1 week discuss with consultant.
For management of hypomagnesaemia see local protocol.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Infertility
Hypersensitivity reactions
Nephrotoxicity

- **Frequently occurring side effects**

Myelosuppression
Nausea and vomiting
Constipation, diarrhoea
Stomatitis and mucositis
Fatigue
Rash
Oedema
Ototoxicity
Electrolyte disturbances

- **Other side effects**

Mild alopecia
Taste disturbances

Significant drug interactions – for full details consult product literature/ reference texts

Warfarin/coumarin anticoagulants: Avoid use due to elevations in INR. Switch to low molecular weight heparin during treatment.

Aminoglycoside antibiotics: increased risk of nephrotoxicity and ototoxicity
Clozapine: increased risk of agranulocytosis, avoid concomitant use
Diuretics: increased risk of nephrotoxicity and ototoxicity
Nephrotoxic drugs: increased nephrotoxicity ; not recommended
Phenytoin: carboplatin reduces absorption and efficacy of phenytoin

Additional comments

Nil

References

- Summary of Product Characteristics Carboplatin (Hospira) accessed 16 November 2017 via www.medicines.org.uk
- Allwood M, Stanley A, Wright P, editors. The cytotoxics handbook. 4th ed. Radcliffe Medical Press. 2002.
- Jeremic B1 et al. Radiation therapy alone or with concurrent low-dose daily either cisplatin or carboplatin in locally advanced unresectable squamous cell carcinoma of the head and neck: a prospective randomized trial. Radiother Oncol. 1997 Apr;43(1):29–37.

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