Carboplatin (breast)

Indication
Treatment of advanced breast cancer, usually after prior treatment with anthracyclines and taxanes.

ICD-10 codes
Codes prefixed with C50.

Regimen details

Day	Drug	Dose	Route
1	Carboplatin	AUC 6*	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. If using an EDTA consider dosing at AUC 5 and if using Cockcroft and Gault consider dosing at AUC 6.
CrCl should be capped at 125mL/min.

Consider starting at a dose of AUC 5 for patients who have been heavily pre-treated or who have significant co-morbidity.

Cycle frequency
21 days

Number of cycles
6 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 - high emetogenic potential

Additional supportive medication

Mouthwashes 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

Baseline EDTA if suspected or significant renal dysfunction.

Investigations - pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	96 hours
U+E (including creatinine)	7 days
LFTs	7 days

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.
If myelosuppression results in delays of subsequent courses reduce dose by 1 x AUC.

Following an episode of febrile neutropenia reduce dose by 1 x AUC for all future doses.

If thrombocytopenia (nadir platelets ≤ 50 x 10^9/L) reduce by 1 x AUC for all future doses.

- **Renal impairment**

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

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

- **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 and reduce dose by 1 x AUC for all future doses. If delays of > 1 week discuss with consultant.
If delays of > 3 weeks or > 2 dose reductions are required, discontinue treatment.

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

- O'Brien ME, Talbot DC, Smith IE. Carboplatin in the treatment of advanced breast cancer. A phase II study using a pharmacokinetically guided dose schedule. J Clin Oncol; 1993: 11; 2112-7.
- Summary of Product Characteristics Carboplatin (Hospira) accessed 29 October 2014 via www.medicines.org.uk
- Allwood M, Stanley A, Wright P, editors. The cytotoxics handbook. 4th ed. Radcliffe Medical Press. 2002.

Written/reviewed by: Dr M Beresford (Consultant Oncologist, Royal United Hospital, Bath)

Checked by: Sarah Murdoch (Senior Oncology Pharmacist, SW Strategic Clinical Network)

Authorised by: Dr J Braybrooke (Consultant Oncologist, UHBristol NHS Trust, SW Strategic Clinical Network)

Date: 14 January 2015