

## Carboplatin and Paclitaxel (oesophagus)

### Indication

Neo-adjuvant treatment for resectable cancer of the oesophagus or oesophagogastric junction.  
WHO performance status 0-2.

### ICD-10 codes

Codes pre-fixed with C15 and C16

### Regimen details

Day	Drug	Dose	Route
1, 8, 15, 22, 29	Paclitaxel	50 mg/m <sup>2</sup>	IV infusion
1, 8, 15, 22, 29	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

Weekly for 5 weeks concurrent with radiotherapy. Starting on the first day of radiotherapy.

### Number of cycles

As above

### Administration

Paclitaxel should be administered first.

Paclitaxel is administered in a 250mL sodium chloride 0.9% non-PVC infusion bag with a 0.22 micron in-line filter over 1 hour. Blood pressure and pulse should be monitored regularly (e.g. every 30 minutes) during paclitaxel infusion.

Carboplatin should be administered in 250mL glucose 5% over 30 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 paclitaxel or 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 re-started 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 paclitaxel or carboplatin and appropriate therapy initiated.

### Pre-medication

30 minutes prior to paclitaxel: chlorphenamine 10mg IV and dexamethasone 8mg IV.

Antiemetics as per local guidelines.

### Emetogenicity

Days 1, 8, 15, 22, 29 have moderate emetic potential.

### Additional supportive medication

H<sub>2</sub> antagonist or proton pump inhibitor if required.

Mouthwashes as per local policy

### Extravasation

Carboplatin – irritant (Group 3)

Paclitaxel - vesicant (Group5)

### 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	Pre day 8, 15, 22, 29. Results valid for 72 hours
U+E (including creatinine)	Pre day 8, 15, 22, 29. Results valid for 72 hours
LFTs	Pre day 8, 15, 22, 29. Results valid for 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	$\geq 1.0 \times 10^9/L$
Platelets	$\geq 50 \times 10^9/L$
Bilirubin	$< 5 \times \text{ULN}$
AST/ALT	$< 5 \times \text{ULN}$
Creatinine Clearance (CrCl)	$> 20 \text{ mL/min}$ (and $< 20\%$ change)

### Dose modifications

- Haematological toxicity**

If on day 8, 15, 22, 29, and 36 the WBC are  $< 1.0 \times 10^9/L$  and/or platelets  $< 50 \times 10^9/L$ , chemotherapy will be delayed by 1 week until recovery above these values.

In case of febrile neutropenia (neutrophils  $< 0.5 \times 10^9/L$  and fever  $> 38.5^\circ\text{C}$ ) or in case of severe bleeding or requiring  $\geq 2$  units of platelet transfusions further chemotherapy will be withheld.

Neutrophils ( $\times 10^9/L$ )		Platelets ( $\times 10^9/L$ )	Dose modification	
			Carboplatin	Paclitaxel
$\geq 1.0$	and	$\geq 50$	100%	100%
$< 1.0$	or	$< 50$	Delay 1 week	Delay 1 week

- Renal impairment**

If calculated CrCl falls by  $>20\%$  from previous dose, consider dose recalculation.

CrCl (mL/min)	Carboplatin dose
> 20	100%
≤ 20	Contra-indicated

- **Hepatic impairment**

Paclitaxel should be used with caution and close monitoring in moderate hepatic impairment and is contraindicated in severe hepatic impairment.

- **Other toxicities**

Any Grade 3-4 toxicity (except mucositis and alopecia) – delay until ≤ Grade 1 toxicity and reduce dose. Discuss with consultant.

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

- **Rare or serious side effects**

Myelosuppression  
 Infertility  
 Teratogenicity  
 Neurotoxicity  
 Hypersensitivity reactions  
 Pulmonary fibrosis  
 Electrolyte disturbances  
 Arrhythmias  
 Cardiac failure

- **Frequently occurring side effects**

Nausea and vomiting  
 Mucositis, stomatitis  
 Myelosuppression  
 Diarrhoea, constipation  
 Peripheral neuropathy  
 Oedema  
 Phlebitis  
 Myalgia, arthralgia  
 Alopecia  
 Fatigue

- **Other side effects**

Elderly patients may have a higher incidence of severe neuropathy, severe myelosuppression, or cardiovascular events compared to younger patients.

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

**Warfarin/coumarin anticoagulants:** increased or fluctuating anticoagulant effects. Avoid if possible, consider switching patient to a low molecular weight heparin during treatment or if the patient continues taking an oral anticoagulant monitor the INR at least once a week and adjust dose accordingly.

**Paclitaxel** is a CYP 2C8/9 and CYP 3A4 substrate. Drug levels may be increased by inhibitors of these enzymes and decreased by inducers of these enzymes.

#### **Carboplatin only:**

**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

Radiotherapy is given as follows: 41.4Gy in 23 fractions, 5 days per week.

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### References

- Summary of Product Characteristics Carboplatin (Hospira) accessed via [www.medicines.org.uk](http://www.medicines.org.uk) (18 June 2014)
- Summary of Product Characteristics Paclitaxel (Hospira) accessed via [www.medicines.org.uk](http://www.medicines.org.uk) (18 June 2014)
- Gaast AV et al, the CROSS Study Group. Effect of preoperative concurrent chemoradiotherapy on survival of patients with resectable esophageal or esophagogastric junction cancer: Results from a multicenter randomized phase III study. Accessed online on:  
[http://www.asco.org/ascov2/Meetings/Abstracts?&vmview=abst\\_detail\\_view&confID=74](http://www.asco.org/ascov2/Meetings/Abstracts?&vmview=abst_detail_view&confID=74)

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