Chemotherapy Protocol

BLADDER

CARBOPLATIN (AUC4.5)-GEMCITABINE

Regimen

- Bladder-Carboplatin-Gemcitabine

Indication

- Locally advanced or metastatic urothelial cancer
- WHO performance status 0,1, 2
- Palliative intent

Toxicity

Drug	Adverse Effect
Carboplatin	Thrombocytopenia, peripheral neuropathy, nephrotoxicity at high doses, electrolyte disturbances
Gemcitabine	Peripheral oedema, diarrhoea, constipation, rash, respiratory problems, influenza like symptoms, radiosensitising

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

Drugs

- FBC, LFTs and U&Es prior to day 1 and 8 of treatment.
- Calculated or measured creatinine clearance prior to each cycle. EDTA may be considered prior to cycle 1 or if there are significant changes in renal function during treatment.

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

Haematological

Consider blood transfusion if the patient is symptomatic of anaemia or has a haemoglobin of less than 8g/dL.

Day 1

Neutrophils ($x10^9$/L)	**Dose Modifications (carboplatin and gemcitabine)**
more than or equal to 1	100%
less than 1	1st Occurrence Delay until recovery. 2nd Occurrence Delay until recovery then give 75% of the original dose.
Febrile Neutropenia	1st Occurrence Delay until recovery and then re-start treatment using 75% of the original dose.
Platelets ($x10^9$/L)	**Dose Modifications (carboplatin and gemcitabine)**
more than or equal to 100	100%
Less than100	1st Occurrence. Delay until recovery then give 75% of the original dose. 2nd Occurrence Delay until recovery then give 50% of the original dose.

Day 8

Neutrophils ($x10^9$/L)	**Dose Modifications (gemcitabine)**
more than or equal to 1	100%
0.5 - 1	75%
less than 0.5	Omit
Platelets ($x10^9$/L)	**Dose Modifications (gemcitabine)**
more than or equal to 100	100%
50 - 100	75%
less than 50	Omit

If dose modifications to gemcitabine dose are required on day 1, continue with reduced dose for day 8.

Hepatic Impairment

Drug	Bilirubin µmol/L		AST/ALT units/L	Dose (% of original dose)
Carboplatin	N/A		N/A	No dose adjustment needed
Gemcitabine	more than 30*		N/A	Initiate treatment with a dose of 800mg/m^2

*Limit reflects local practice and may vary from published sources

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Carboplatin	less than 20	Omit
Gemcitabine	more than or equal to 30	100%
	less than 30	Consider dose reduction

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

For all other non-haematological NCI-CTC grade 3 and above toxicities delay treatment until the adverse effect has resolved to NCI-CTC grade 1 or below. The dose of the causative agent should then be reduced to 75% of the original dose or discontinued as appropriate.

Regimen

21 day cycle for 6 cycles

Drug	Dose	Days	Administration
Carboplatin	AUC 4.5	1	Intravenous infusion in 500ml Glucose 5% over 60 minutes
Gemcitabine	1000mg/m^2	1 and 8	Intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

Dose Information

- Carboplatin dose will be dose banded in accordance with the national dose bands (10mg/ml)
- Gemcitabine will be dose banded in accordance with the national dose bands (38mg/ml).

Administration Information

Extravasation

- Carboplatin – irritant
- Gemcitabine – neutral

Additional Therapy

- Antiemetics

  15-30 minutes prior to chemotherapy on **day 1**

  - dexamethasone 8mg oral or intravenous
  - ondansetron 8mg oral or intravenous

  As take home medication on **day 1**

  - dexamethasone 4mg oral twice a day for 3 days
  - metoclopramide 10mg oral three times a day for 3 days then as required (supply for day 1 and 8)

  15-30 minutes prior to chemotherapy on **day 8**

  - metoclopramide 10mg oral or intravenous

- Mouthwashes according to local or national policy on the treatment of mucositis
- Gastric protection with a proton pump inhibitor or a H_2 antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

References
1.Linardou H, Aravantinos G, Efstathiou E et al. Gemcitabine and carboplatin combination as first line treatment in elderly patients and those unfit for cisplatin-based chemotherapy with advanced bladder carcinoma: phase II study of the Hellenic Co-operative Oncology Group. Urology 2004; 64 (3): 479-484.
2.Carles J, Nogue M, Domenech M et al. Carboplatin – gemcitabine treatment of patients with transitional cell carcinoma of the bladder and impaired renal function. Onc 2000;59:24-27

REGIMEN SUMMARY

Carboplatin (AUC4.5)-Gemcitabine

Day 1

1. Dexamethasone 8mg oral or intravenous
   Administration instructions: Administer 15-30 minutes prior to SACT

2. Ondansetron 8mg oral or intravenous
   Administration instructions: Administer 15-30 minutes prior to SACT

3. Gemcitabine 1000mg/m^2 intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes.

4. Carboplatin AUC4.5 intravenous infusion in 500ml glucose 5% over 60 minutes.

Take Home Medicines

5. Dexamethasone 4mg oral twice a day for 3 days starting on day two of the cycle

6. Metoclopramide 10mg oral three times a day for 3 days then when required
   Administration Instructions
   Please supply 10 days or an original pack if appropriate to cover day 1 and 8

Day 8

7. Metoclopramide 10mg oral or intravenous
   Administration instructions: Administer 15-30 minutes prior to SACT

8. Gemcitabine 1000mg/m^2 intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.2	May 2023	Carboplatin and gemcitabine changed to national dose banding Coding removed	Alexandra Pritchard Pharmacist	Tom Hurst Pharmacy Technician
1.1	May 2015	"(AUC4.5) added to title Header changed Metoclopramide dose changed to 10mg Bolus removed from intravenous bolus throughout text Comment re local bilirubin limit added Mucositis recommendation changed Dexamethasone TTO clarified Metoclopramide TTO clarified Disclaimer added	Donna Kimber Pharmacy Technician	Rebecca Wills Pharmacist
1	Dec 2012	None	Rebecca Wills Pharmacist Dr Deborah Wright Pharmacist	Dr Joanna Gale Consultant Medical Oncologist Dr Mathew Wheater Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury Hospitals NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.