

Chemotherapy Protocol

BLADDER

CISPLATIN (70)-GEMCITABINE

Regimen

Bladder-Cisplatin (70)-Gemcitabine

Indication

First line treatment of locally advanced or metastatic urothelial cancer

Adjuvant / Neo-adjuvant treatment of urothelial cancer

WHO performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Cisplatin	Neuropathy, nephrotoxicity, ototoxicity
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 patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL.

Day 1

Neutrophils (x10⁹/L)	Dose Modifications (cisplatin and gemcitabine)
1 or greater	100%
less than 1	1 st Occurrence. Delay until recovery 2 nd Occurrence Delay until recovery then give 75% of the original dose
Febrile Neutropenia	1 st Occurrence Delay until recovery and then re-start treatment using 75% of the original dose
Platelets (x10⁹/L)	Dose Modifications (cisplatin and gemcitabine)
100 or greater	100%
Less than 100	1 st Occurrence. Delay until recovery then give 75% of the original dose 2 nd Occurrence Delay until recovery then give 50% of the original dose

Day 8

Neutrophils (x10⁹/L)	Dose Modifications (gemcitabine)
1 or greater	100%
0.5 - 1	75%
less than 0.5	Omit
Platelets (x10⁹/L)	Dose Modifications (gemcitabine)
100 or greater	100%
50 - 100	75%
less than 50	Omit

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

Hepatic Impairment

Drug	Bilirubin μmol/L	AST/ALT units/L	Dose (% of original dose)
Cisplatin	N/A	N/A	No dose adjustment needed
Gemcitabine	30 or greater*	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)
Cisplatin	60 or greater	100%
	40-59	Consider cisplatin (35)- gemcitabine (split dose cisplatin)
	39 or below	Consider alternative
Gemcitabine	30 or greater	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 3 - 6 cycles (3 cycles will be set in Aria)

First line treatment - 6 cycles

Adjuvant - 4 cycles

Neoadjuvant - 3 cycles

Drug	Dose	Days	Administration
Cisplatin	70mg/m ²	1	Intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride at a rate of cisplatin of 1mg/min (minimum 120 minutes)
Gemcitabine	1000mg/m ²	1 and 8	Intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

Dose Information

- Cisplatin will be dose banded according to the CSCCN agreed bands
- Gemcitabine will be dose banded according to the CSCCN agreed bands

Administration Information

Extravasation

- Cisplatin – exfoliant
- Gemcitabine – neutral

Additional Therapy

- Antiemetics

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

- aprepitant 125mg oral
- dexamethasone 4mg oral or intravenous
- ondansetron 8mg oral or intravenous

As take home medication on **day 1**

- aprepitant 80mg oral daily for on days 2 and 3
- dexamethasone 4mg oral once a day for 3 days
- metoclopramide 10mg oral three times a day as required (supply for day 1 and 8)
- ondansetron 8mg oral twice a day for 3 days

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

- metoclopramide 10mg oral or intravenous

- Cisplatin pre and post hydration as follows

Pre

Furosemide 40mg oral or intravenous

1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes

Post

1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes

Patients should be advised to drink at least 3 litres of fluid in the 24 hours after administration of cisplatin.

- Mouthwashes according to local or national policy on the treatment of mucositis
- Gastric protection with a proton pump inhibitor or a H₂ antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

[Coding \(OPCS 4.6\)](#)

- Procurement – X70.5
- Delivery – X72.1 & X72.4

References

- 1.Hussain SA, Stocken DD, Riley P et al. A phase I/II study of gemcitabine and fractionated cisplatin in an outpatient setting using a 21 day schedule in patients with advanced and metastatic bladder cancer. Br J Cancer 2004; 91 (5): 844-849.
- 2.von der Maase, Hansen SW, Roberts JT et al. Gemcitabine and cisplatin versus methotrexate, vinblastine, doxorubicin and cisplatin in advanced or metastatic bladder cancer: results of a large randomised multinational multicentre phase III study. J Clin Oncol 2000; 18 (17): 3068-3077.
- 3.Dash A, Pettus JA, Herr HW, et al. A Role for Neoadjuvant Gemcitabine Plus Cisplatin in MuscleInvasive Urothelial Carcinoma of the Bladder: A Retrospective Experience. Cancer 2008;113:2471–7.

REGIMEN SUMMARY

Cisplatin (70)-Gemcitabine

Cycle One and Two

Day 1

1. Aprepitant 125mg oral
2. Dexamethasone 4mg oral or intravenous
3. Ondansetron 8mg oral or intravenous
4. Furosemide 40mg oral or intravenous
5. Sodium chloride 0.9% 1000ml with magnesium sulphate 16mmol and potassium chloride 20mmol intravenous infusion over 60 minutes
6. Gemcitabine 1000mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes
7. Cisplatin 70mg/m² in 1000ml sodium chloride 0.9% with 20mmol potassium chloride intravenous infusion at a rate of cisplatin of 1mg/min (minimum 120 minutes)
8. Sodium chloride 0.9% 1000ml with magnesium sulphate 16mmol with potassium chloride 20mmol intravenous infusion over 60 minutes

Take Home Medicines

9. Aprepitant 80mg once a day on days 2 and 3 oral
10. Dexamethasone 4mg once a day for 3 days oral starting on day two of the chemotherapy
11. Metoclopramide 10mg three times a day when required for nausea oral
Administration Instructions
Please supply 10 days or an original pack if appropriate to cover Day 1 and Day 8.
12. Ondansetron 8mg twice a day for 3 days oral starting on the evening of day one of treatment

Day 8

13. Metoclopramide 10mg oral or intravenous
14. Gemcitabine 1000mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

Cycle Three

Day 1

15. Warning – check number of cycles
16. Aprepitant 125mg oral
17. Dexamethasone 4mg oral or intravenous
18. Ondansetron 8mg oral or intravenous
19. Furosemide 40mg oral or intravenous
20. Sodium chloride 0.9% 1000ml with magnesium sulphate 16mmol and potassium chloride 20mmol intravenous infusion over 60 minutes
21. Gemcitabine 1000mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes.
22. Cisplatin 70mg/m² in 1000ml sodium chloride 0.9% with 20mmol potassium chloride intravenous infusion at a rate of cisplatin of 1mg/min (minimum 120 minutes)
23. Sodium chloride 0.9% 1000ml with magnesium sulphate 16mmol with potassium chloride 20mmol intravenous infusion over 60 minutes

Take Home Medicines

24. Aprepitant 80mg once a day on days 2 and 3 oral
25. Dexamethasone 4mg once a day for 3 days oral starting on day two of the chemotherapy
26. Metoclopramide 10mg three times a day when required for nausea oral
Administration Instructions
Please supply 10 days or an original pack if appropriate to cover Day 1 and Day 8.
27. Ondansetron 8mg twice a day for 3 days oral starting on the evening of day one of treatment

Day 8

28. Metoclopramide 10mg oral or intravenous
29. Gemcitabine 1000mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	May 2015	Header changed Comment re local bilirubin limit added Metoclopramide dose changed to 10mg Bolus removed from intravenous bolus throughout text Mucositis recommendation changed Dexamethasone TTO clarified Ondansetron TTO clarified Metoclopramide TTO removed from day 8, supply on day 1 increased. 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 Wheeler 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.