Gemcitabine-Cisplatin split-day schedule (Bladder Cancer)

Northern Cancer Alliance

DRUG ADMINISTRATION SCHEDULE

Day	Drug	Dose	Route	Diluent	Rate
1	Sodium Chloride 0.9%	1000ml	IV	Pre-hydration	2 hours
	Ondansetron	8mg	Oral /Slow bolus/15 min infusion		
	Dexamethasone	8mg	Oral /Slow Bolus		
	Furosemide	20mg	ORAL	If no contra-indication	
	Gemcitabine*	**1250mg/m^2**	**IV**	**250ml Sodium Chloride 0.9%**	**30 minutes**
	Cisplatin	**35mg/m^2**	**IV**	**500ml Sodium Chloride 0.9%**	**1 hour**
	20mmol Potassium and 10mmol Magnesium	1000ml	IV	Sodium Chloride 0.9%	2 hours
8	Sodium Chloride 0.9%	1000ml	IV	Pre-hydration	2 hours
	Ondansetron	8mg	Oral /Slow bolus/15 min infusion		
	Dexamethasone	8mg	Oral /Slow Bolus		
	Furosemide	20mg	ORAL	If no contra-indication	
	Gemcitabine*	**1250mg/m^2**	**IV**	**250ml Sodium Chloride 0.9%**	**30 minutes**
	Cisplatin	**35mg/m^2**	**IV**	**500ml Sodium Chloride 0.9%**	**1 hours**
	20mmol Potassium and 10mmol Magnesium	1000ml	IV	Sodium Chloride 0.9%	2 hours

*Ondansetron IV must be infused over 15 minutes in patients over 65 years of age.

Hydration schedules may be modified according to local agreement.
Note: A Gemcitabine dose of 1000mg/m^2 has also been used in this regimen, either dose is acceptable.

CYCLE LENGTH AND NUMBER OF DAYS

21 Day cycle for 3 cycles for neoadjuvant patients
21 Day cycle for 6 cycles for metastatic patients

APPROVED INDICATIONS

Transitional cell carcinoma (TCC) of the urothelium

EXCLUSION CRITERIA

- Inadequate haematological function
- Inadequate renal function (GFR < 50ml/min)

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PRE-MEDICATION

Furosemide

Adequate hydration and urinary flow is essential when administering cisplatin. Ideally patients should be weighed (with bladder empty) prior to commencing treatment and to use 20 mg of Oral or IV Furosemide as a diuretic given routinely if there is no contraindication. Alternatively, urine output should be measured with a target output of > 100ml/hour. Patient should be re-weighed at the end of cisplatin (with empty bladder) and consideration given to administering a further dose of Furosemide if weight gain is more than 1.5 Kg.

RECOMMENDED TAKE HOME MEDICATION

Ondansetron 8mg twice daily for up to 3 days
Dexamethasone 4mg twice daily for up to 3 days
Metoclopramide 10 mg three times daily as required
(For day 8, only metoclopramide will usually be needed)
Suggested antiemetic regimen - may vary with local practice. See CINV policy for more details

INVESTIGATIONS / MONITORING REQUIRED

Prior to first cycle:
FBC, U&Es (Calculated CrCl, or measured GFR), LFTs, Mg & Ca,

Prior to each cycle: U&Es, LFTs, Mg, FBC, CrCl.

Check renal function before commencing platinum. Use EDTA or Wright to calculate GFR. GFR should usually be above 60 ml/min for cisplatin-based treatment. If GFR < 60 ml/min discuss with an Oncology Specialist.

ASSESSMENT OF RESPONSE

Radiologically (half way through treatment) and tumour markers (each cycle).

REVIEW BY CLINICIAN

Prior to each cycle, unless being reviewed by a Nurse Specialist or Pharmacist under a locally agreed framework.

NURSE / PHARMACIST LED REVIEW

As per locally agreed framework.

ADMINISTRATION NOTES

- Maintain oral intake of 1-2 litres of fluids for 6 hours after IV fluids are discontinued. Magnesium Sulfate and Potassium Chloride are required due to the renal toxicity of Cisplatin resulting in excess loss.
- Gemcitabine is a radio-sensitiser – use with caution if receiving concomitant radiotherapy.

TOXICITIES

Common: Nausea & Vomiting, Fatigue, Alopecia, Emesis, Myelosuppression, Skin Rash
Less Common: Tinnitus, Nephrotoxicity, Peripheral Neuropathy, Metallic Taste, Hearing Impairment

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DOSE MODIFICATION / TREATMENT DELAYS

Neurotoxicity

Grade	Cisplatin Dose
1	100%
2	50%
3 or 4	Omit

Haematological Toxicity:

Delay treatment if ANC < 1.5 x 10^9 cells/l or PLT < 100 x 10^9 cells/l on days 1 or 8.

Renal Function:

Cisplatin is renally excreted, dose modification of cisplatin should be considered when CrCl is less that 50ml/min.

CrCl (or GFR)	Cisplatin
> 60ml/min	100%
51 – 60ml/min	75%
40 - 50ml/min	50%
40 - 30 ml/min	Contra-indicated
10 - 30ml/min	Contra-indicated
< 10ml/min	Contra-indicated

Hepatic Function:

Gemcitabine toxicity increases when Bilirubin is > 28µmol/l – consideration of a 25% dose reduction may be appropriate.

TREATMENT LOCATION

Suitable for administration as a day case in cancer units (with experience in administering cisplatin) and cancer centres.

Reference:

1. Advanced Bladder Cancer (ABC). Meta-analysis collaboration neoadjuvant chemotherapy in invasive bladder cancer - a systematic review and meta-analysis. Lancet 2003; 361: 1927-1934.
2. von der Maase H, 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. Hussain, S.A., Palmer, D.H., Lloyd, B., Collins, S.I., Barton, D., Ansari, J. and James, N.D., 2012. A study of split-dose cisplatin-based neo-adjuvant chemotherapy in muscle-invasive bladder cancer. Oncology letters, 3(4), pp.855-859.

Document Control

Document Title:	Gemcitabine-Cisplatin split-day schedule (Bladder Cancer)		
Document No:	CRP17-U021	**Current Version:**	1.0
Reviewer:	Chris Beck Chemotherapy Pharmacist Northern Cancer Alliance	**Date Approved:**	13.03.18
Approved by:	Steve Williamson Consultant Pharmacist Northern Cancer Alliance	**Due for Review**	13.03.21
Summary of Changes	1.0	New draft adapted from Gem-Cis protocol.	