

Gemcitabine (1000mg/m²) and CISplatin (70mg/m²) Therapy- 28 day

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	*Reimbursement Indicator
Treatment of patients with locally advanced or metastatic transitional cell carcinoma (TCC) of the urothelium	C67	00282a	

**If a reimbursement indicator (e.g. ODMS, CDS) is not defined, the drug and its detailed indication have not been assessed through the formal HSE reimbursement process.*

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patient's individual clinical circumstances.

Gemcitabine is administered on day 1, 8 and 15 and CISplatin is administered on day 1 following gemcitabine or day 2 of each 28 day cycle for 4-6 cycles unless disease progression or unacceptable toxicity develops.

Facilities to treat anaphylaxis MUST be present when the chemotherapy is administered.

Admin. Order	Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	1,8 and 15	Gemcitabine	1000mg/m ²	IV infusion	250ml NaCl 0.9% over 30mins	Every 28 days
2	1	*CISplatin	70mg/m ²	IV infusion	1000ml NaCl 0.9% over 120mins	Every 28 days

*Pre and post hydration therapy required for CISplatin

See local hospital policy recommendations.

Suggested prehydration for CISplatin therapy:

- Administer 10mmol magnesium sulphate (MgSO₄) ((+/-KCl 20mmol/L if indicated) in 1000 mL sodium chloride 0.9% over 60 minutes.

Administer CISplatin as described above

Post hydration: Administer 1000 ml 0.9% NaCl over 60mins

Mannitol 10% may be used to as per local policy to induce diuresis, although there is no conclusive evidence that this is required. The routine use of furosemide to increase urine flow is not recommended unless there is evidence of fluid overload.

ELIGIBILITY:

- Indications as above
- ECOG 0-2
- Adequate marrow reserve (ANC > 1.5 x 10⁹/L, platelets > 100x10⁹/L)

EXCLUSIONS:

- Hypersensitivity to gemcitabine, CISplatin or any of the excipients
- CISplatin
 - Pre existing neuropathies ≥ grade 2
 - Creatinine clearance < 60 mL/min
 - Significant hearing impairment/tinnitus

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- Breast Feeding

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Audiometry and creatinine clearance as clinically indicated

Regular tests:

- Day 1: FBC, renal and liver profile
- Day 8: FBC, creatinine

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant.

Haematological:

Prior to commencing a new treatment cycle (i.e day 1), ANC must be $>1 \times 10^9/L$ and platelets $> 100 \times 10^9/L$

Dose modifications for gemcitabine within a cycle (i.e day 8)

Table 1: Dose modifications for gemcitabine within a cycle (i.e days 8 and 15)

ANC ($\times 10^9 /L$)		Platelet count ($\times 10^9 /L$)		Other toxicity	Recommended dose of Gemcitabine
>1	and	> 100			100 %
0.5- 1	or	50-100			75%
< 0.5	or	<50			Omit. Do not restart treatment until ANC > 0.5 and platelets > 50
ANC < 0.5 for > 5 days or ANC < 0.1 for > 3 days or Any incidence of febrile neutropenia	or	< 25	or	cycle delay of >1 week due to any toxicity	Reduce dose to 75% of the original cycle initiation dose for all subsequent cycles.

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Renal and Hepatic Impairment:

Table 2: Dose modification of CISplatin and Gemcitabine in renal and hepatic impairment

Drug	Renal Impairment		Hepatic Impairment
	Cr Cl (ml/min)	Dose	
CISplatin	≥60	100%	No dose reductions necessary
	45-59	75%	
	<45	Consider CARBOplatin- Clinical decision	
Gemcitabine	>30	100%	AST elevations do not seem to cause dose limiting toxicities. If bilirubin > 27 µmol/L, initiate treatment with dose of 800 mg/m ² .
	<30	Consider dose reduction clinical decision	

Management of adverse events:

Table 3: Dose Modification of gemcitabine and CISplatin for Adverse Events

Adverse reactions	Recommended dose modification
Grade ≥ 3 Non-haematological toxicity (except nausea/vomiting)	Therapy with gemcitabine and CISplatin should be withheld (until toxicity has resolved to grade ≤ 1) and may be resumed with dose reduction at discretion of prescribing consultant.
Grade ≥ 2 peripheral neuropathy	Substitute CARBOplatin AUC 5 or 50% reduction of CISplatin dose after recovery to grade ≤ 1. 100% dose of gemcitabine

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

CISplatin High (Refer to local policy)
 Gemcitabine Low (Refer to local policy).

PREMEDICATIONS:

Pre and Post Hydration therapy required for CISplatin administration (Reference local policy or see recommendations above).

OTHER SUPPORTIVE CARE:

Patient should be encouraged to drink large quantities of liquids for 24 hours after the cisplatin infusion to ensure adequate urine secretion.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

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

- **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated appropriately.
- **Renal Toxicity:** Nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside antibiotics. Irreversible renal failure associated with

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hemolytic uremic syndrome may occur (rare) with gemcitabine. Use caution with pre-existing renal dysfunction.

- **Pulmonary Toxicity:** Acute shortness of breath may occur. Discontinue treatment if drug-induced pneumonitis is suspected.
- **Cardiovascular:** Due to the risk of cardiac and/or vascular disorders with gemcitabine, particular caution must be exercised with patients presenting a history of cardiovascular events.

Please refer to NCCP protocol 00283 Gemcitabine Monotherapy-Locally Advanced or metastatic for detailed information on adverse effects/regimen specific complications relating to gemcitabine

DRUG INTERACTIONS:

- CISplatin may potentiate the nephrotoxic and ototoxic effects of loop diuretics and aminoglycosides so concurrent use should be avoided.
- Current drug interaction databases should be consulted for more information.

ATC CODE:

Gemcitabine	L01BC05
CISplatin	L01XA01

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Version	Date	Amendment	Approved By
1			Prof Maccon Keane
2	15/11/2017	Updated title and dosing in renal and hepatic impairment. Applied new NCCP regimen template	

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

ⁱ ODMS – Oncology Drug Management System

CDS – Community Drug Schemes (CDS) including the High Tech arrangements of the PCRS community drug schemes

Further details on the Cancer Drug Management Programme is available at;

<http://www.hse.ie/eng/services/list/5/cancer/profinfo/medonc/cdmp/>

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