Gemcitabine (1000mg/m^2) and CISplatin (25mg/m^2) Therapy - 21 day

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
Locally advanced or metastatic pancreatic carcinoma	C25	00383a	N/A
Locally advanced or metastatic biliary tree carcinoma	C22/C23	00383b	N/A

*For post 2012 indications only

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 patients individual clinical circumstances.

Gemcitabine and CISplatin are administered on day 1 and day 8 of a 21 day cycle and treatment is continued until disease progression or unacceptable toxicity develops.

Facilities to treat anaphylaxis MUST be present when systemic anti-cancer therapy (SACT) is administered.

Admin. Order	Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	1 and 8	Gemcitabine	1000mg/m^2	IV infusion	250mL NaCl 0.9% over 30 minutes	Every 21 days
2	1 and 8	[1]CISplatin	25mg/m^2	IV infusion	1000mL NaCl 0.9% over 60 minutes	Every 21 days

[1]**Prehydration therapy required for CISplatin**
See local hospital policy recommendations.
Suggested prehydration for CISplatin therapy:

1. Administer 10mmol magnesium sulphate (MgSO4) (+/-KCl 10-20mmol/L if indicated) in 1000mL NaCl 0.9% over 60 – 120 minutes. (Refer to relevant local hospital policy for advice on administration of electrolyte infusions).

Administer CISplatin as described above

ELIGIBILITY:

- Indications as above
- ECOG 0-2
- Adequate marrow reserve (ANC >1.5x10^9/L, platelets >100x10^9/L)
- Total bilirubin ≤ 1.5xULN, liver enzymes ≤ 5xULN

EXCLUSIONS:

- Hypersensitivity to gemcitabine, CISplatin or any of the excipients
- Patients with inadequate renal function (CrCl <45mL/min)
- Breastfeeding

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:

Table 1: Dose modification of Gemcitabine in haematological toxicity

ANC (x10^9/L)		Platelets (x10^9/L)	Dose
≥1.0	and	>100	100% Dose
0.5 to 0.99	or	50-100	75%
<0.5	or	<50	Omit*
*CISplatin also omitted			

Renal and Hepatic Impairment:

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

Drug	Renal Impairment		Hepatic Impairment
	CrCl (mL/min)	Dose	No dose reductions necessary
CISplatin	>60	100%	
	45-59	50%	
	<45	Delay*	
Gemcitabine	>30	100%*	If bilirubin ≥27 micromol/L, use dose of 800 mg/m^2 and increase dose to full dose if tolerated.
	<30	Consider dose reduction. Clinical decision.	
*Delay both Cisplatin and gemcitabine if day 1; if day 8, omit CISplatin			

Management of adverse events:

Table 3: Dose Modification schedule 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	Omit CISplatin or consider substituting CISplatin with CARBOplatin 100% dose of gemcitabine
Grade ≥ 2 pneumonitis	Discontinue gemcitabine

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

- As outlined in NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting - Available on the NCCP website

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

For information:
Within NCIS regimens, antiemetics have been standardised by the Medical Oncologists and Haemato-oncologists. Information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) - Available on the NCCP website
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) - Available on the NCCP website

PREMEDICATIONS:

Pre Hydration therapy required for CISplatin administration **(Refer to 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:

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details.

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for information.

REFERENCES:

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2. Valle JW, Wasan H et al; CISplatin plus gemcitabine versus gemcitabine for biliary tract cancer. N Engl J Med 2010;362(14):1273-81.
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https://www.eviq.org.au/clinical-resources/side-effect-and-toxicity-management/prophylaxis-and-prevention/184-nephrotoxicity-associated-with-CISplatin

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12. CISplatin 1mg/mL Concentrate for Solution for Infusion. Summary of Product Characteristics. Last updated: 13/10/2021. Accessed Oct 2021. Available at: https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA0822-199-001_13102021113634.pdf
13. Gemcitabine 40mg/mL Concentrate for Solution for Infusion Summary of Product Characteristics. Last updated: 02/09/2021. Accessed Oct 2021. Available at: https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA1380-182-001_02102020144836.pdf

Version	Date	Amendment	Approved By
1			Prof Maccon Keane
2	15/11/2017	Updated title, CISplatin hydration and dosing in renal and hepatic	Prof Maccon Keane

		impairment. Applied new NCCP regimen template	
3	06/11/2019	Reviewed. Update of adverse events, emetogenic potential	Prof Maccon Keane
4	10/12/2020	Update of renal and hepatic dose modification table	
5	18/11/2021	Updated CISplatin prehydration. Updated Dose modification of gemcitabine in haematological toxicity and in renal and hepatic impairment. Updated adverse effects.	Prof Maccon Keane
6	08/02/2024	Amended CISplatin infusion volume Updated suggested hydration therapy for cisplatin	Prof Maccon Keane
7	16/10/2024	Updated infusion time for CISplatin. Updated Table 1-Dose modification of gemcitabine in haematological toxicity. Updated regimen in line with NCCP standardisation.	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.