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

## INDICATIONS FOR USE:

| INDICATION | ICD10 | Regimen Code | Reimbursement Status |
|---|---|---|---|
| Locally advanced or metastatic pancreatic carcinoma | C25 | 00383a | Hospital |
| Locally advanced or metastatic biliary tree carcinoma | C22/C23 | 00383b | Hospital |

## 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 the chemotherapy 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 30mins | Every 21 days |
| 2 | 1 and 8 | [1]CISplatin | 25mg/m$^2$ | IV infusion | 500ml NaCl 0.9% over 120mins | Every 21 days |

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

1. Administer 10mmol magnesium sulphate ($MgSO_4$) (+/-KCl 10-20mmol/L if indicated) in 1000 mL sodium chloride 0.9% over 60 minutes.

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 | <75 | 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 |
|---|---|---|---|
| | **Cr Cl (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<br>100% dose of gemcitabine |
| Grade ≥ 2 pneumonitis | Discontinue gemcitabine |

# SUPPORTIVE CARE:

## EMETOGENIC POTENTIAL:

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

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

**Gemcitabine:**

- **Pulmonary Toxicity**: Acute shortness of breath may occur. Discontinue treatment with gemcitabine 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.
- **Infusion time:** Infusion time prolonged beyond 60 minutes has been shown to increase volume of distribution and has been associated with an increase in toxicity. However, given in the context of a fixed dose rate (FDR) regimen, prolonged infusions have also been reported to produce a higher response rate than standard regimens in association with a higher intracellular accumulation of its active metabolite (dFdCTP) (8-11).

**CISplatin:**

- Ototoxicity and sensory neural damage should be assessed by history prior to each cycle**.**

## 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.

## REFERENCES:


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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 impairment. Applied new NCCP regimen template | Prof Maccon Keane |
| 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 |

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.