# Cisplatin and Gemcitabine (biliary tract)

## Indication

Palliative treatment of metastatic or locally advanced /unresectable biliary tract cancers including gall bladder carcinomas and cholangiocarcinomas.

WHO performance status 0-2.

## ICD-10 codes

Codes prefixed with C23.

## Regimen details

| Day | Drug | Dose | Route |
|---|---|---|---|
| 1 and 8 | Cisplatin | 25mg/m$^2$ | IV infusion |
| 1 and 8 | Gemcitabine | 1000mg/m$^2$ | IV infusion |

## Cycle frequency

21 days

## Number of cycles

6 - 8 cycles

## Administration

Cisplatin is administered in 500mL sodium chloride 0.9% over 60 minutes following the pre and post hydration protocol below.

| Infusion Fluid & Additives | Volume | Infusion Time |
|---|---|---|
| Sodium Chloride 0.9% + 2g $MgSO_4$ + 20mmol KCl | 1000mL | 1 hour |
| ***Ensure urine output > 100mL / hour prior to giving cisplatin. Give a single dose of furosemide 20mg iv if necessary.*** | | |
| Cisplatin | 500mL | 1 hour |
| Sodium Chloride 0.9% | 500mL | 30 minutes |
| **TOTAL** | **2000mL** | **2 hours 30 minutes** |

Note: Patients with low magnesium or low potassium should have 2g $MgSO_4$ and 20mmol KCl added to the post-hydration bag, the volume increased to 1000mL and the duration of the infusion increased to 2 hours.

All patients must be advised to drink at least 2 litres of fluid over the following 24 hours.

Gemcitabine is administered in 250-500mL sodium chloride 0.9% over 30 minutes.

## Pre-medication
Hydration regimen as above.

## Emetogenicity
This regimen has a moderate - high emetogenic potential

## Additional supportive medication
Mouthwashes as per local policy.
Loperamide if required.

## Extravasation
Cisplatin is an exfoliant (Group 4)
Gemcitabine is neutral (Group 1)

## Investigations – pre first cycle

| **Investigation** | **Validity period** (or as per local policy) |
|---|---|
| FBC | 14 days |
| U+E (including creatinine) | 14 days |
| LFTs | 14 days |
| Magnesium | 14 days |
| Calcium | 14 days |

## Investigations – pre subsequent cycles

| **Investigation** | **Validity period** (or as per local policy) |
|---|---|
| FBC | 96 hours |
| U+E (including creatinine) | 7 days |
| LFTs | 7 days |
| Magnesium | 7 days |
| Calcium | 7 days |

Additional FBC is required on day 8.

## Standard limits for administration to go ahead
If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

| **Investigation** | **Limit** |
|---|---|
| Neutrophils | > 1.0 x $10^9$/L |
| Platelets | > 100 x $10^9$/L |
| Bilirubin | < 1.5 x ULN |
| Creatinine Clearance (CrCl) | ≥ 45mL/min |

## Dose modifications

- **Haematological toxicity**

| **Neutrophils** (x$10^9$/L) | | **Platelets** (x $10^9$/L) | **Cisplatin dose** | **Gemcitabine dose** |
|---|---|---|---|---|
| >1.0 | and | >100 | 100% | 100% |
| 0.5-1.0 | or | 50-100 | 100% | 75% |
| <0.5 | or | <50 | omit | omit |

In the case of febrile neutropenia restart cisplatin at 100% and gemcitabine at 75% dose.

- **Renal impairment**

| **CrCl** (mL/min) | **Cisplatin dose** | **Gemcitabine dose** |
|---|---|---|
| ≥ 45 | 100% | 100% |
| 30-44 | Omit* | 100% |
| < 30 | Omit* | Consider dose reduction (consultant decision) |

*consider switching to carboplatin AUC 2 if CrCl < 45ml/min.

- **Hepatic impairment**

Lack of information available on the use of gemcitabine in patients with hepatic impairment, therefore, used with caution. If bilirubin > 1.5 x ULN, consider reducing dose to 800mg/m$^2$ (consultant decision).

- **Other toxicities**

Neurotoxicity or ototoxicity:

- ≥ Grade 2: permanently stop cisplatin and switch to carboplatin AUC 2.

Stomatitis:

- Grade 3: reduce gemcitabine to 75% dose.

## Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Infertility
Interstitial pneumonitis
Nephrotoxicity

- **Frequently occurring side effects**

Myelosuppression
Nausea and vomiting
Constipation
Stomatitis and mucositis
Peripheral neuropathy
Fatigue
Rash
Oedema
Ototoxicity

- **Other side effects**

Skin reactions
Nail changes
Taste disturbances

## Significant drug interactions – for full details consult product literature/ reference texts

**Warfarin/coumarin anticoagulants:** Avoid use due to elevations in INR. Switch to low molecular weight heparin during treatment.

**Allopurinol and antigout agents**: Cisplatin may increase the concentration of blood uric acid. Thus, in patients concurrently receiving **antigout agents** such as allopurinol, colchicine, probenecid or sulfinpyrazone, dosage adjustment of these drugs may be necessary to control hyperuricemia and gout.

**Cisplatin**:
Avoid ototoxic and nephrotoxic agents (including aminoglycosides, loop diuretics and amphotericin B) as these may increase toxicity of cisplatin.

## Additional comments

Nil

## References


- Summary of Product Characteristics Cisplatin (Hospira) accessed 25 June 2014 via www.medicines.org.uk
- Summary of Product Characteristics gemcitabine (Lilly) accessed 25 June 2014 via www.medicines.org.uk
- Allwood M, Stanley A, Wright P, editors. The cytotoxics handbook. 4th ed. Radcliffe Medical Press. 2002.
- Daniels S. North London Cancer Network. Dose adjustment for cytotoxics in hepatic impairment accessed 31 July 2014 via www.bopawebsite.org.uk
- Heinemann V; Quietzsch D; Gieseler F, Gonnermann M, Schönekäs H, Rost A, et al Randomized phase III trial of gemcitabine plus cisplatin compared with gemcitabine alone in advanced pancreatic cancer. J Clin Oncol 2006;24(24):3946-52.



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