Gemcitabine (1000mg/m^2) Monotherapy - 56 day

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Treatment of patients with locally advanced or metastatic adenocarcinoma of the pancreas	C25	00283a	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 is administered once weekly for up to 7 weeks followed by a week of rest (1 cycle = 56 days). Subsequent cycles should consist of injections once weekly for 3 consecutive weeks out of every 4 weeks until disease progression or unacceptable toxicity develops.
Facilities to treat anaphylaxis MUST be present when the chemotherapy is administered.

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1, 8, 15, 22, 29, 36, 43	Gemcitabine	1000mg/m^2	IV infusion	250ml NaCl 0.9% over 30mins	Cycle 1 (56 days)
1, 8 and 15	Gemcitabine	1000mg/m^2	IV infusion	250ml NaCl 0.9% over 30mins	Cycle 2 onwards (28 days)

ELIGIBILITY:

- Indication as above
- ECOG 0-2
- Macroscopic complete resection of tumour
- Adequate marrow reserve (ANC > 1.5 x 10^9/L, platelets > 100x10^9/L)
- Adequate renal (creatinine ≤ 1.5xULN) and liver (bilirubin level ≤ 2.0 mg/dL [34.2 micromol/L], AST and ALT ≤ 3 x ULN) function

EXCLUSIONS:

- Hypersensitivity to gemcitabine or any of the excipients
- Breast feeding

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist

TESTS:

Baseline tests:

- FBC, renal and liver profile

Regular tests:

- FBC prior to each treatment
- Renal and liver profile prior to each cycle

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 x 10^9/L and platelets > 100 x 10^9/L

Table 1: Dose modifications for gemcitabine for haematological toxicity on treatment day

ANC (x 10^9 /L)		Platelet count (x 10^9 /L)		Recommended dose of Gemcitabine
>1	and	> 100		100 %
0.5- 1	or	50-100		75% or delay based on clinical assessment
< 0.5	or	<50		Delay

Renal and Hepatic Impairment:

Table 2: Dose modification of gemcitabine in renal and hepatic impairment

Drug	Renal Impairment		Hepatic Impairment
Gemcitabine	Cr Cl (ml/min	Dose	If bilirubin ≥27 micromol/L, use dose of 800 mg/m^2 and increase dose to full dose if tolerated.
	>30	100%	
	<30	Consider dose reduction. Clinical decision.	

Management of adverse events:

Table 3: Dose Modification of gemcitabine for Adverse Events

Adverse reactions	Recommended dose modification
Grade > 3 Non-haematological toxicity (except nausea/vomiting)	Therapy with gemcitabine should be withheld (until toxicity has resolved to grade ≤ 1) and may be resumed with 50% dose reduction or treatment discontinued at discretion of prescribing consultant.
Grade > 4 Non-haematological toxicity	Discontinue treatment.

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:
Gemcitabine: Low **(Refer to local policy)**

PREMEDICATIONS: None usually required

OTHER SUPPORTIVE CARE: No specific recommendations

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.
- **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.
- **Irreversible renal failure** associated with haemolytic uraemic syndrome may occur rarely with gemcitabine. Use caution with pre-existing renal impairment.
- **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) (3-7).

DRUG INTERACTIONS:

- Current drug interaction databases should be consulted for more information.

REFERENCES:

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11. Gemcitabine 40 mg/ml Concentrate for Solution for Infusion Summary of Product Characteristics Accessed Nov 2021. Available at: https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA2059-039-002_18042019163628.pdf

Version	Date	Amendment	Approved By
1			Prof Maccon Keane
2	06/12/2017	Updated title, indications, dosing for haematological toxicity and dosing in renal and hepatic impairment. Applied new NCCP regimen template	Prof Maccon Keane
3	31/08/2018	Updated treatment table and dosing modifications for haematological toxicity	Prof Maccon Keane
4	09/09/2020	Regimen reviewed	Prof Maccon Keane
5	18/10/2021	Reviewed. Amended eligibility (liver function) and dose modification in hepatic impairment.	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.