Gemcitabine (1000mg/m^2) and RT therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Non-metastatic, locally advanced pancreatic cancer	C25	00521a	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 in 3 cycles over ten weeks as described in the treatment table below.

The summary table for the administration of gemcitabine and radiotherapy describes the three cycles as below:

1. Cycle 1 consists of Gemcitabine administered on days 1 and 8 of a 21 day cycle.
2. Cycle 2 (chemoradiotherapy phase) consists of gemcitabine administered on days 1, 8, and 15 of a 28-day cycle concurrent with radiotherapy on days 1 through 5, 8 through 12, and 15 through 19.
3. Cycle 3 consists of Gemcitabine administered on days 1 and 8 of a 21 day cycle.

Facilities to treat anaphylaxis MUST be present when gemcitabine is administered.

Treatment table for Gemcitabine:

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1 and 8	Gemcitabine	1000mg/m^2	IV infusion	250ml NaCl 0.9% over 30mins	1 (21 day cycle)
1,8,15	Gemcitabine	1000mg/m^2	IV infusion	250ml NaCl 0.9% over 30mins	2 (concurrently with radiation on day 1-5 and 8-12 and 15-19) (28 day cycle)
1 and 8	Gemcitabine	1000mg/m^2	IV infusion	250ml NaCl 0.9% over 30mins	3 (21 day cycle)

Summary table for administration of gemcitabine and radiotherapy

Cycle number	1 (21 day)			2 (28 day)				3 (21 day)		
Day number	1	8	15	1	8	15	22	1	8	15
Treatment with gemcitabine	✓	✓	✗	✓	✓	✓	✗	✓	✓	✗
Radiotherapy	No radiotherapy			Radiotherapy on days 1-5 and 8-12 and 15-19				No radiotherapy		

ELIGIBILITY:

- Indications as above
- ECOG 0-2

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 within a cycle (i.e day 8 and 15)

ANC (x 10^9 /L)		Platelet count (x 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.

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**	AST elevations do not seem to cause dose limiting toxicities. If bilirubin > 27 micromol/L, initiate treatment with dose of 800 mg/m^2.
	≥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 ≥ 2 Pneumonitis	**Discontinue gemcitabine**
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.

DRUG INTERACTIONS:

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

ATC CODE:

Gemcitabine L01BC05

REFERENCES:

1. Small W, Berlin J et al. Full-Dose Gemcitabine With Concurrent Radiation Therapy in Patients With Nonmetastatic Pancreatic Cancer:A Multicenter Phase II Trial. J Clin Oncol 26:*942-947. © 2008*
2. Gemcitabine 100 mg/ml Concentrate for Solution for Infusion Summary of Product Characteristics Accessed October 2020 . Available at https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA2315-092-004_25062020164320.pdf
3. Dosage Adjustment for Cytotoxics in Renal Impairment January 2009; North London Cancer Network. Available at http://londoncancer.org/media/65600/renal-impairment-dosage-adjustment-for-cytotoxics.pdf
4. Dosage Adjustment for Cytotoxics in Hepatic Impairment January 2009;North London Cancer Network. Available at http://londoncancer.org/media/65594/hepatic-impairment-dosage-adjustment-for-cytotoxics.pdf

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1	07/11/2018		Prof Maccon Keane
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