Gemcitabine (400mg/m^2) and RT therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Resectable Adenocarcinoma of the head of Pancreas	C25	00522a	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 on day 5 of a 7 day cycle for 7 consecutive weeks (total number of doses is 7) according to the treatment table below
Cycle 2 and 3 consist of gemcitabine administered on day 5 concurrent with radiation administered on days 1 through 5 of a 7-day cycle according to the summary table below.

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

Treatment table for Gemcitabine:

Day	Drug	Dose	Route	Diluent & Rate	Cycle
5	Gemcitabine	400mg/m^2	IV infusion	250ml NaCl 0.9% over 30mins	Repeat every 7 days for 7 weeks

Summary table for administration of gemcitabine and radiotherapy:

Week	Monday Day 1	Tuesday Day2	Wednesday Day 3	Thursday Day 4	Friday Day 5
1					Gemcitabine
2	**Radiotherapy**	**Radiotherapy**	**Radiotherapy**	**Radiotherapy**	Gemcitabine & **Radiotherapy**
3	**Radiotherapy**	**Radiotherapy**	**Radiotherapy**	**Radiotherapy**	Gemcitabine & **Radiotherapy**
4					Gemcitabine
5					Gemcitabine
6					Gemcitabine
7					Gemcitabine

ELIGIBILITY:

- Indications as above
- ECOG 0-2

EXCLUSIONS:

- Hypersensitivity to gemcitabine or any of the excipients
- Pregnancy or lactation

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:

Table 1: Dose modifications for gemcitabine

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, consider dose reduction. Clinical decision
	≥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.

REFERENCES:

1. Douglas B. Evans, Gauri R. Varadhachary Preoperative Gemcitabine-Based Chemoradiation for Patients With Resectable Adenocarcinoma of the Pancreatic Head. J Clin Oncol 2008;26:3496-3502
2. Oettle H, Neuhaus P et al. Adjuvant chemotherapy with gemcitabine and long-term outcomes among patients with resected pancreatic cancer: the CONKO-001 randomized trial. JAMA. 2013;310(14) :1473-8**1.**
3. Gemcitabine 40 mg/ml Concentrate for Solution for Infusion Summary of Product Characteristics Accessed Jan 2021. Available at: https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA2059-039-004_30092019160211.pdf
4. Dosage Adjustment for Cytotoxics in Renal Impairment January 2009; North London Cancer Network.
5. Dosage Adjustment for Cytotoxics in Hepatic Impairment January 2009;North London Cancer Network.
6. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V2 2019. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf

Version	Date	Amendment	Approved By
1	07/11/2018		Prof Maccon Keane
2	30/01/2019	Clarification of dosing in hepatic impairment	Prof Maccon Keane
3	10/02/2021	Amended exclusions	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.