Gemcitabine (100mg/m^2) and Radiotherapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
Treatment of muscle-invasive transitional cell urothelial bladder cancer	C67	00759	N/A

* This applies to post 2012 indications

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 days 1, 8, 15, and 22 of a 28-day cycle for 1 cycle, with concurrent radiotherapy. Gemcitabine is administered 2 to 4 hours before radiotherapy.

Facilities to treat anaphylaxis MUST be present when systemic anti-cancer therapy (SACT) is administered.

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1, 8, 15 and 22	Gemcitabine	100mg/m^2	IV infusion	250mL NaCl 0.9% over 30 minutes	Every 28 days for 1 cycle

Note: Administration volumes and fluids have been standardised to facilitate electronic prescribing system builds.

ELIGIBILITY:

- Indications as above
- ECOG 0-2
- Adequate haematological and organ function

EXCLUSIONS:

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

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist.

TESTS:

Baseline tests:

- FBC, renal and liver profile

Regular tests:

- Weekly FBC, renal and liver profile at end of 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.
- Patients should have an ANC ≥ 1.5 x 10^9/L and platelet count of ≥ 100 x 10^9/L prior to the initiation of a cycle.

Haematological:

Patients should have an ANC ≥ 1.5 x 10^9/L and platelet count of ≥ 100 x 10^9/L prior to the initiation of a cycle.

Table 1: Dose modification of gemcitabine in haematological toxicity

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[a]	**CrCl (mL/min**	**Dose**	**Total bilirubin (µmol/L)**	**Dose**
	≥30	No dose adjustment is needed	<27	No dose adjustment is needed
	<30	No need for dose adjustment is expected	≥27	Either start at 80% of the original dose and increase the dose if tolerated or start with full dose with active monitoring

[a] Gemcitabine: Renal and hepatic recommendations from Giraud et al 2023

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:

- As outlined in NCCP Classification Document for Systemic AntiCancer Therapy (SACT) Induced Nausea and Vomiting linked- Available on NCCP website

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

For information:
Within NCIS regimens, antiemetics have been standardised by Medical Oncologists and Haemato-oncologists and information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) - Available on the NCCP website
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) - Available on the NCCP website

PREMEDICATIONS: None usually required

OTHER SUPPORTIVE CARE: No specific recommendations

ADVERSE EFFECTS:

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details.

DRUG INTERACTIONS:

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

REFERENCES:

1. Choudhury A et al. Phase II study of conformal hypofractionated radiotherapy with concurrent gemcitabine in muscle-invasive bladder cancer. J Clin Oncol. 2011 Feb 20;29(6):733-8. doi: 10.1200/JCO.2010.31.5721. Epub 2011 Jan 4. PMID: 21205754.
2. Giraud E L, Lijster B D, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. Available at: https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(23)00216-4/fulltext
3. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V5 2023. 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
4. Gemcitabine 40mg/mL Concentrate for Solution for Infusion. Summary of Product Characteristics. Last updated 14/12/2023. Accessed July 2024. Available at: https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA1986-122-001_14122023101810.pdf

Version	Date	Amendment	Approved By
1	25/11/2024		Dr. Ray McDermott

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.