Gemcitabine (1250mg/m^2) Monotherapy - 21 day[i]

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Loco-regionally recurrent/metastatic nasopharyngeal cancer not amenable for local curative therapy.	C11	00514a	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.

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

Gemcitabine is administered once weekly for 2 consecutive weeks followed by a 1 week pause (1 cycle = 21 days) for a maximum of 6 cycles or until disease progression or unacceptable toxicity develops.

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1 and 8	Gemcitabine	1250mg/m^2	IV infusion	250ml NaCl 0.9% over 30mins	Every 21 days

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 ≥1.0 x 10^9/L and platelets ≥100 x 10^9/L.

Table 1: Dose modifications for gemcitabine within a cycle (i.e day 8)

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 3a: 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:** In association 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. Foo, KF, Tan EH, Leong SS, et al. Gemcitabine in metastatic nasopharyngeal carcinoma of the undifferentiated type. Ann Oncol 2002;13:150-156.
2. EVIQ Protocol Summary for Nasopharyngeal recurrent or metastatic Gemcitabine- Using Protocol code 1510 revised October 2016.
3. BCCA Protocol Summary for Treatment of Loco-regionally Recurrent/Metastatic Nasopharyngeal Cancer not Amenable for Local Curative Therapy with Gemcitabine. Using Gemcitabine Protocol code HNNAVGEM revised November 2012
4. Gemcitabine 1g Powder for Solution for Infusion Summary of Product Characteristics Accessed Oct 2020. Available at http://www.hpra.ie/img/uploaded/swedocuments/FINAL_PA2315-092-002_27022019151618.pdf
5. 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

6. 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

Version	Date	Amendment	Approved By
1	07/11/2018		Prof Maccon Keane
2	23/10/2020	Reviewed	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

[i] This indication is outside the licensed indications for Gemcitabine in Ireland. Patients should be informed of the unlicensed nature of this indication and consented to treatment in line with the hospital's policy on the use of unlicensed medication and unlicensed or "off label" indications. Prescribers should be aware of their responsibility in communicating any relevant information to the patient and also in ensuring that the unlicensed or "off label" indication has been acknowledged by the hospital's Drugs and Therapeutics Committee, or equivalent, in line with hospital policy.