Gemcitabine (1000mg/m^2) and CISplatin (80mg/m^2) Induction Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement Status*
Induction chemotherapy prior to concurrent chemo-radiotherapy for loco-regionally advanced nasopharyngeal carcinoma.	C11	00903a	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 on day 1 and day 8 and CISplatin is administered on day 1 of a 21 day cycle for a maximum of 3 cycles.

This treatment is followed by chemoradiation commencing 21 to 28 days after the first day of the last cycle of induction chemotherapy.

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

Admin. Order	Day	Drug	Dose	Route	Diluent & Rate	Cycle 1-3
1	1 and 8	Gemcitabine	1000mg/m^2	IV infusion	250mL NaCl 0.9% over 30 minutes	Every 21 days
2	1	*CISplatin	80mg/m^2	IV infusion	1000mL NaCl 0.9% over 60 minutes	Every 21 days

***Pre and post hydration therapy required for CISplatin**

See local hospital policy recommendations.

Suggested prehydration for CISplatin therapy:

Administer 10mmol magnesium sulphate ($MgSO_4$) ((+/-KCl 20mmol/L if indicated) in 1000mL NaCl 0.9% over 60-120 minutes. (Refer to relevant local hospital policy for advice on administration of electrolyte infusions).

Administer CISplatin as described above

Post hydration: Administer 1000mL 0.9% NaCl over 60 minutes

Mannitol 10% may be used as per local policy to induce diuresis, although there is no conclusive evidence that this is required. The routine use of furosemide to increase urine flow is not recommended unless there is evidence of fluid overload.

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

ELIGIBILITY:

- Indications as above
- ECOG 0-2
- Adequate marrow reserve (ANC > 1.5 x 10^9/L, platelets > 100x10^9/L)

EXCLUSIONS:

- Hypersensitivity to Gemcitabine, CISplatin or any of the excipients
- CISplatin
  - Pre-existing neuropathies ≥ grade 2
  - Pre-existing renal impairment CrCl <60mL/min
  - Significant hearing impairment/tinnitus
- Pregnancy or breastfeeding

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Audiology as clinically indicated

Regular tests:

- Day 1: FBC, renal and liver profile
- Day 8: FBC

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 and CISplatin in haematological toxicity

ANC x 10 /L (pre-treatment blood test)	Dose modification
1.0 to < 1.5	Treatment should continue if patient is clinically well
0.5 to < 1.0	Delay treatment until recovery, consider GCSF
< 0.5	Delay treatment until recovery and reduce CISplatin and gemcitabine by 25% for subsequent cycles, consider GCSF
Febrile neutropenia or previous delay for myelosuppression	Delay treatment until recovery and reduce CISplatin and gemcitabine by 25% for subsequent cycles, consider GCSF
Prolonged recovery greater than two weeks delay or 3 delay for myelosuppression	Clinical decision
Platelets x 10 /L (pre-treatment blood test)	
75 to < 100	The general recommendation is to delay, however if the patient is clinically well it may be appropriate to continue treatment; refer to treating team and/or local policy
50 to < 75	Delay treatment until recovery
<50	Delay treatment until recovery and reduce CISplatin and gemcitabine by 25% for subsequent cycles
If treatment needs to be delayed on Day 8, it should be omitted rather than delayed and the next treatment planned for the originally scheduled date if recovered	

Renal and Hepatic Impairment:

Table 2: Dose modification of CISplatin and Gemcitabine in renal and hepatic impairment

Drug	Renal Impairment		Hepatic Impairment	
CISplatin	**CrCl (mL/min)**	**Dose**	No need for dose adjustment is expected	
	50-59	65mg/m^2		
	40-49	50mg/m^2		
	<40	Not recommended		
	Haemodialysis	Clinical decision.		
Gemcitabine	**CrCl (mL/min)**	**Dose**	**Bilirubin micromol/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
Renal and hepatic dose modifications as per Giraud et al 2023				

Management of adverse events:

Table 3: Dose Modification of Gemcitabine and CISplatin for Adverse Events

Adverse reactions	Recommended dose modification
Grade ≥ 2 Non-haematological toxicity (except nausea/vomiting)	Therapy with Gemcitabine and CISplatin should be withheld (until toxicity has resolved to grade ≤ 1) and may be resumed with dose reduction at discretion of prescribing consultant.
Grade ≥ 2 peripheral neuropathy	Dose reduction at the discretion of treating clinician of CISplatin dose after recovery to grade ≤ 1, 100% dose of Gemcitabine
• Severe cutaneous adverse reactions (SCARs) e.g. Stevens-Johnson syndrome (SJS),toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) and acute generalised exanthematous pustulosis (AGEP) • Pulmonary toxicity • Haemolytic syndrome	Discontinue gemcitabine

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

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

CISplatin: High **(Refer to local policy)**
Gemcitabine: Low **(Refer to local policy).**

For information:
Within NCIS regimens, antiemetics have been standardised by the Medical Oncologists and Haemato-oncologists. 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:

- Hydration pre and post CISplatin administration **(Refer to local policy or see recommendations above).**
- Patient should be encouraged to drink large quantities of liquids for 24 hours after the CISplatin infusion to ensure adequate urine secretion.

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 information.

REFERENCES:

1. Zhang, Y. *et al*. Gemcitabine and Cisplatin Induction Chemotherapy in Nasopharyngeal Carcinoma. N Engl J Med. 2019 381(12):1124-1135
2. Irish Medication Safety Network: Best Practice Guidelines For the Safe Use of Intravenous Potassium in Irish Hospitals Available at: https://imsn.ie/wp-content/uploads/2020/10/IMSN-Best-Practice-Guideline-on-IV-Potassium-Oct-2020-approved.pdf
3. Prevention and management of cisplatin induced nephrotoxicityEviQ ID: 184 v.4. Available at: https://www.eviq.org.au/clinical-resources/side-effect-and-toxicity-management/prophylaxis-and-treatment/184-prevention-and-management-of-cisplatin-induced
4. Perazella MA et al. CISplatin nephrotoxicity. UptoDate. Last updated April 2024. Available at: https://www.uptodate.com/contents/cisplatin-nephrotoxicity?search=portilla%20cisplatin&source=search_result&selectedTitle=4%7E150&usage_type=default&display_rank=4
5. 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
6. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V6 2025. 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
7. CISplatin 1mg/mL Concentrate for Solution for Infusion. Summary of Product Characteristics Accessed May 2025. Available at: https://www.medicines.ie/medicines/cisplatin-1-mg-ml-concentrate-for-solution-for-infusion-latex-free-vial-stopper--35271/spc
8. Gemcitabine 1g powder for solution for Infusion. Summary of Product Characteristics Accessed May 2025. Available at: https://assets.hpra.ie/products/Human/27516/Licence_PA2315-092-002_23012024174158.pdf

Version	Date	Amendment	Approved By
1	12/11/2025		Dr Colm Mac Eochagain

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.