

## Gemcitabine (1250mg/m<sup>2</sup>) and CISplatin (75mg/m<sup>2</sup>) Therapy- 21 day

### INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC)	C34	00281a	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 patient's 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 4-6 cycles or until disease progression or unacceptable toxicity develops.

Facilities to treat anaphylaxis MUST be present when the chemotherapy is administered.

Admin. Order	Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	1 and 8	Gemcitabine	1250mg/m <sup>2</sup>	IV infusion	250ml NaCl 0.9% over 30mins	Every 21 days
2	1	*CISplatin	75mg/m <sup>2</sup>	IV infusion	1000ml NaCl 0.9% over 120mins	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<sub>4</sub>) ((+/-KCl 20mmol/L if indicated) in 1000mL sodium chloride 0.9% over 60 minutes.

Administer CISplatin as described above

Post hydration: Administer 1000ml 0.9% NaCl over 60mins

Mannitol 10% may be used to 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 (4,5).

### ELIGIBILITY:

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

### EXCLUSIONS:

- Hypersensitivity to gemcitabine, CISplatin or any of the excipients
- CISplatin
  - Pre existing neuropathies ≥ grade 2

NCCP Regimen: Gemcitabine (1250mg/m <sup>2</sup> )and CISplatin (75mg/m <sup>2</sup> )-21 day	Published: 15/11/2015 Review: 06/11/2021	Version number: 3
Tumour Group: Lung NCCP Regimen Code: 00281	ISMO Contributor: Prof Maccon Keane	Page 1 of 5

The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician, and is subject to HSE's terms of use available at <http://www.hse.ie/eng/Disclaimer>

*This information is valid only on the day of printing, for any updates please check [www.hse.ie/NCCPchemoregimens](http://www.hse.ie/NCCPchemoregimens)*

- Creatinine clearance < 60mL/min
- Significant hearing impairment/tinnitus
- Breast Feeding

## PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist

## TESTS:

### Baseline tests:

- FBC, renal and liver profile
- Audiometry and creatinine clearance as clinically indicated

### Regular tests:

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

### 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 >1x10<sup>9</sup>/L and platelets >100x10<sup>9</sup>/L

Dose modifications for **gemcitabine within a cycle** (i.e Day 8):

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

ANC (x10 <sup>9</sup> /L)		Platelet count (x10 <sup>9</sup> /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 <b>or</b> ANC <0.1 for >3 days <b>or</b> Any incidence of febrile neutropenia	<b>or</b>	<25	<b>or</b>	cycle delay of >1 week due to any toxicity	Reduce dose to 75% of the original cycle initiation dose for all subsequent cycles.

NCCP Regimen: Gemcitabine (1250mg/m <sup>2</sup> )and CISplatin (75mg/m <sup>2</sup> )-21 day	Published: 15/11/2015 Review: 06/11/2021	Version number: 3
Tumour Group: Lung NCCP Regimen Code: 00281	ISMO Contributor: Prof Maccon Keane	Page 2 of 5
<p>The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician, and is subject to HSE's terms of use available at <a href="http://www.hse.ie/eng/Disclaimer">http://www.hse.ie/eng/Disclaimer</a></p> <p><i>This information is valid only on the day of printing, for any updates please check <a href="http://www.hse.ie/NCCPchemoregimens">www.hse.ie/NCCPchemoregimens</a></i></p>		

## Renal and Hepatic Impairment:

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

Drug	Renal Impairment		Hepatic Impairment
	CrCl (ml/min)	Dose	
CISplatin	>60	100%	No dose reductions necessary
	45-59	75%	
	<45	Consider CARBOplatin-Clinical decision	
Gemcitabine	>30	100%	AST elevations do not seem to cause dose limiting toxicities. If bilirubin > 27 micromol/L, initiate treatment with dose of 800mg/m <sup>2</sup> .
	<30	Consider dose reduction clinical decision	

## Management of adverse events:

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

Adverse reactions	Recommended dose modification
Grade ≥ 3 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	Substitute CARBOplatin AUC 5 or 50% reduction of CISplatin dose after recovery to grade ≤ 1. 100% dose of gemcitabine
Grade ≥ 2 pneumonitis	Discontinue gemcitabine

## SUPPORTIVE CARE:

### EMETOGENIC POTENTIAL:

CISplatin High (**Refer to local policy**)

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

### PREMEDICATIONS:

Pre and Post Hydration therapy required for CISplatin administration (**Reference local policy or see recommendations above**).

### OTHER SUPPORTIVE CARE:

Patient should be encouraged to drink large quantities of liquids for 24 hours after the CISplatin infusion to ensure adequate urine secretion.

NCCP Regimen: Gemcitabine (1250mg/m <sup>2</sup> )and CISplatin (75mg/m <sup>2</sup> )-21 day	Published: 15/11/2015 Review: 06/11/2021	Version number: 3
Tumour Group: Lung NCCP Regimen Code: 00281	ISMO Contributor: Prof Maccon Keane	Page 3 of 5
<p>The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician, and is subject to HSE's terms of use available at <a href="http://www.hse.ie/eng/Disclaimer">http://www.hse.ie/eng/Disclaimer</a></p> <p><i>This information is valid only on the day of printing, for any updates please check <a href="http://www.hse.ie/NCCPchemoregimens">www.hse.ie/NCCPchemoregimens</a></i></p>		

## 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.
- **Renal Toxicity:** Nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside antibiotics. Irreversible renal failure associated with hemolytic uremic syndrome may occur (rare) with gemcitabine. Use caution with pre-existing renal dysfunction.
- **Pulmonary Toxicity:** Acute shortness of breath may occur with gemcitabine. 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.

Please refer to NCCP protocol 00283 Gemcitabine Monotherapy-Locally Advanced or metastatic for detailed information on adverse effects/regimen specific complications relating to gemcitabine

## DRUG INTERACTIONS:

- CISplatin may potentiate the nephrotoxic and ototoxic effects of loop diuretics and aminoglycosides so concurrent use should be avoided.
- Current drug interaction databases should be consulted for more information.

## ATC CODE:

Gemcitabine	L01BC05
CISplatin	L01XA01

## REFERENCES:

1. Scagliotti GV, De Marinis F, Rinaldi M, et al. Phase III randomized trial comparing three platinum-based doublets in advanced non-small-cell lung cancer. *J Clin Oncol* 2002;20(21):4285-91.
2. Zatloukal P, et al. Gemcitabine plus cisplatin vs. gemcitabine plus carboplatin in stage IIIb and IV non-small cell lung cancer: a phase III randomized trial. *Lung Cancer* 2003;41(3):321-31.
3. Van Moorsel CJA, Peters GJ, Pinedo HM. Gemcitabine: Future prospects of single-agent and combination studies. *The Oncologist* 1997;2:127-34.
4. Nephrotoxicity Associated with CISplatin EviQ ID: 184 v.3  
<https://www.eviq.org.au/clinical-resources/side-effect-and-toxicity-management/prophylaxis-and-prevention/184-nephrotoxicity-associated-with-CISplatin>
5. Portilla D et al. CISplatin nephrotoxicity. UptoDate Accessed Oct 2017  
[https://www.uptodate.com/contents/CISplatin-nephrotoxicity?source=search\\_result&search=CISplatin%20hydration&selectedTitle=1~150](https://www.uptodate.com/contents/CISplatin-nephrotoxicity?source=search_result&search=CISplatin%20hydration&selectedTitle=1~150)
6. 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>

NCCP Regimen: Gemcitabine (1250mg/m <sup>2</sup> )and CISplatin (75mg/m <sup>2</sup> )-21 day	Published: 15/11/2015 Review: 06/11/2021	Version number: 3
Tumour Group: Lung NCCP Regimen Code: 00281	ISMO Contributor: Prof Maccon Keane	Page 4 of 5
<p>The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician, and is subject to HSE's terms of use available at <a href="http://www.hse.ie/eng/Disclaimer">http://www.hse.ie/eng/Disclaimer</a></p> <p><i>This information is valid only on the day of printing, for any updates please check <a href="http://www.hse.ie/NCCPchemoregimens">www.hse.ie/NCCPchemoregimens</a></i></p>		

7. 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>
8. Cisplatin 1mg/ml Concentrate for Solution for Infusion. Summary of Product Characteristics Last updated: 11/03/2019. Accessed Nov 2019. Available at <https://www.hpra.ie/img/uploaded/swedocuments/Final%20approved%20SPC%20PA0822.199.001.pdf>
9. Gemcitabine 40mg/ml Concentrate for Solution for Infusion Summary of Product Characteristics Last updated: 30/09/2019. Accessed Nov 2019. Available at [https://www.hpra.ie/img/uploaded/swedocuments/Licence\\_PA2059-039-004\\_30092019160211.pdf](https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA2059-039-004_30092019160211.pdf)
10. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V1 2018. Available at: <https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp%20antiemetic%20classification%20document%20v1%202018.pdf>

Version	Date	Amendment	Approved By
1			Prof Maccon Keane
2	15/11/2017	Updated title, suggested CISplatin hydration and dosing in renal and hepatic impairment. Applied new NCCP regimen template	Prof Maccon Keane
3	06/11/2019	Reviewed. Update of adverse events.	Prof Maccon Keane

Comments and feedback welcome at [oncologydrugs@cancercontrol.ie](mailto:oncologydrugs@cancercontrol.ie).

NCCP Regimen: Gemcitabine (1250mg/m <sup>2</sup> )and CISplatin (75mg/m <sup>2</sup> )-21 day	Published: 15/11/2015 Review: 06/11/2021	Version number: 3
Tumour Group: Lung NCCP Regimen Code: 00281	ISMO Contributor: Prof Maccon Keane	Page 5 of 5
<p>The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibly of the prescribing clinician. and is subject to HSE's terms of use available at <a href="http://www.hse.ie/eng/Disclaimer">http://www.hse.ie/eng/Disclaimer</a></p> <p><i>This information is valid only on the day of printing, for any updates please check <a href="http://www.hse.ie/NCCPchemoregimens">www.hse.ie/NCCPchemoregimens</a></i></p>		