CISplatin (100mg/m^2) with Radiotherapy (RT)-21 day

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Chemoradiation treatment for locally advanced (stage III to IV) squamous cell carcinoma (SCC) of the head and neck	C76	00387a	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.

CISplatin is administered once every 21 days with concurrent radiotherapy for 3 cycles.

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

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	CISplatin	100mg/m^2	IV Infusion	1000ml NaCl 0.9% over 2 hours (Pre and Post hydration therapy required)**	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 10-20mmol/L if indicated) in 1000 mL sodium chloride 0.9% over 60 minutes (3).

Administer CISplatin as described above
Post hydration: Administer 1000 ml 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).

CISplatin (radiosensitizer) – Radiotherapy
Since CISplatin is used in this regimen as a radiosensitising agent, it is to be administered on a day on which radiotherapy is delivered. Radiotherapy should start after CISplatin infusion is completed. If radiotherapy is cancelled on the CISplatin day, do not give CISplatin that day and postpone chemotherapy until radiation therapy resumes.

ELIGIBILITY:

- Indications as above
- ECOG 0-2
- Adequate hepatic, renal, and bone marrow function

EXCLUSIONS:

- Hypersensitivity to CISplatin or any of the excipients
- Moderate/severe renal impairment (creatinine clearance < 60 mL/min)
- Significant hearing impairment/tinnitus
- Pregnancy
- Lactation

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist

TESTS:

Baseline tests:

- FBC, liver and renal profiles
- Audiology and creatinine clearance if clinically indicated.

Regular tests:

- FBC, liver and renal profiles 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 modification of CISplatin in haematological toxicity

ANC ($x10^9$/L)		Platelets ($x10^9$/L)	Dose
≥1.5	**and**	≥ 100	100%
1 -1.49	**or**	75-99	75%
<1	**or**	<75	Delay chemoradiation until recovery

Renal and Hepatic Impairment:

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

Renal Impairment		Hepatic Impairment
CrCl (ml/min)	**Dose**	No dose modifications for hepatic impairment
≥60	100%	
45-59	75%	
<45	Hold CISplatin or delay with additional IV fluids	

Management of adverse events:

Table 3: Dose Modification of CISplatin for Adverse Events

Adverse reactions	Recommended dose modification
Peripheral neuropathy Grade 2 Grade 3 or 4	 Reduce CISplatin dose by 25% Omit CISplatin

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: High (**Refer to local policy).**

PREMEDICATIONS:

Hydration pre and post CISplatin administration **(Reference local policy or see recommendations above).**

OTHER SUPPORTIVE CARE:

Prior to initiation of treatment, patients should be referred for consultation to Dentistry and Nutrition Services.

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 is common with CISplatin. Encourage oral hydration.
- Ototoxicity and sensory neural damage should be assessed by history prior to each cycle**.**

DRUG INTERACTIONS:

- Avoid concurrent use of CISplatin with nephrotoxic drugs (e.g. aminoglycosides, furosemide, NSAIDS) due to additive nephrotoxicity. If necessary monitor renal function closely.
- Current drug interaction databases should be consulted for more information.

REFERENCES:

1. Forastiere AA, Zhang Q, Weber RS et al. Long-term results of RTOG 91-11: a comparison of three nonsurgical treatment strategies to preserve the larynx in patients with locally advanced larynx cancer. J Clin Oncol. 2013; 31(7):845.
2. Forastiere AA, Goepfert H, Maor M et al. Concurrent chemotherapy and radiotherapy for organ preservation in advanced laryngeal cancer. N Engl J Med. 2003;349(22):2091
3. Irish Medication Safety Network: Best Practice Guidelines for the Safe Use of Intravenous Potassium in Irish Hospitals. Published Oct 2020. Available at: https://imsn.ie/wp-content/uploads/2020/10/IMSN-Best-Practice-Guideline-on-IV-Potassium-Oct-2020-approved.pdf
4. Nephrotoxicity Associated with CISplatin EviQ ID: 184 v.3 https://www.eviq.org.au/clinical-resources/side-effect-and-toxicity-management/prophylaxis-andprevention/184-nephrotoxicity-associated-with-CISplatin 4.
5. Portilla D et al. CISplatin nephrotoxicity. UptoDate Accessed Oct 2017 https://www.uptodate.com/contents/cisplatin-nephrotoxicity?search=cisplatin%20nephrotoxicity&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1
6. Dosage Adjustment for Cytotoxics in Renal Impairment January 2009; North London Cancer Network.
7. Cisplatin 1mg/ml Concentrate for Solution for Infusion. Summary of Product Characteristics Accessed Oct 2020. Available at https://www.hpra.ie/img/uploaded/swedocuments/Final%20approved%20SPC%20PA0822.199.001.pdf

Version	Date	Amendment	Approved By
1	20/12/2016		Prof Maccon Keane
2	26/11/2018	Updated to new NCCP template. Updated with revised hydration regimen for CISplatin	Prof Maccon Keane
3	10/11/2020	Reviewed	Prof Maccon Keane
4	02/09/2021	Updated cisplatin hydration recommendation	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.