CISplatin (40mg/m^2) Weekly with Radiotherapy (RT)

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	*Reimbursement Indicator
Chemoradiation treatment for locally advanced (stage IIB to IVA) cervical squamous cell carcinoma (SCC)	C53	00385a	
Chemoradiation treatment for locally advanced bladder cancer	C67	00385b	
Chemoradiation treatment for locally advanced nasopharnygeal carcinoma	C11	00385c	
Chemoradiation treatment for locally advanced unresectable head and neck squamous carcinoma (SCC) in patients who cannot tolerate three weekly CISplatin regimens.	C76	00385d	

**If a reimbursement indicator (e.g. ODMS, CDS[i]) is not defined, the drug and its detailed indication have not gone through the formal reimbursement process as legislated for in the Health (Pricing and Supply of Medical Goods) Act 2013.*

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.

Cervical Carcinoma: CISplatin is administered once every 7 days with concurrent radiotherapy for 5 cycles and can be continued weekly with concurrent radiotherapy at the discretion of the prescribing consultant.
Bladder, Nasopharnygeal, Head and Neck: CISplatin is administered once every 7 days with concurrent radiotherapy for 6 cycles.

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

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	CISplatin	40mg/m^2	IV Infusion	500-1000ml NaCl 0.9% over 2 hours (Pre and Post hydration therapy required)**	Every 7 days

**** Pre and post hydration therapy required for CISplatin**
See local hospital policy recommendations.
Suggested prehydration for CISplatin therapy:

1. Administer 10mmol magnesium sulphate ($MgSO_4$) ((+/-KCl 20mmol/L if indicated) in 1000 mL sodium chloride 0.9% over 60 minutes.

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 (9,10).

CISplatin (radiosensitizer) – Radiotherapy Since CISplatin is used in this protocol as a radiosensitising agent, it is to be administered on the 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.

ELIGIBILTY:

- 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
- Breast Feeding

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist

TESTS:

Baseline tests:

- Blood, renal and liver profile
- Audiology and creatinine clearance if clinically indicated

Regular tests:

- Blood, 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:

Table 1: Dose modification of CISplatin in haematological toxicity

ANC ($x10^9$ /L)		Platelets ($x10^9$ /L)	Dose
<1	**or**	<100	Delay chemoradiation until recovery

Renal and Hepatic Impairment:

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

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

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: 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.
- **Renal toxicity:** 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.

ATC CODE:

CISplatin L01XA01

REFERENCES:

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3. Kim YS, Shin SS, et al . Prospective randomized comparison of monthly fluorouracil and cisplatin versus weekly cisplatin concurrent with pelvic radiotherapy and high-dose rate brachytherapy for locally advanced cervical cancer. Gynecol Oncol. 2008;108(1):195.

4. Rose, P. G., S. Ali, E. Watkins, et al. Longterm followup of a randomized trial comparing concurrent single agent cisplatin, cisplatin based combination chemotherapy, or hydroxyurea during pelvic irradiation for locally advanced cervical cancer: a Gynecologic Oncology Group Study. J Clin Oncol 2007;25(19):2804-2810.
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Version	Date	Amendment	Approved By
1			Prof Maccon Keane
2	20/09/2017	Applied new NCCP regimen template Clarified dosing in Cervical Carcinoma	Prof Maccon Keane
3	06/12/2017	Updated with revised CISplatin hydration regimen recommendations	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

[i] ODMS – Oncology Drug Management System
CDS – Community Drug Schemes (CDS) including the High Tech arrangements of the PCRS community drug schemes
Further details on the Cancer Drug Management Programme is available at;
http://www.hse.ie/eng/services/list/5/cancer/profinfo/medonc/cdmp/