Cisplatin and Radiotherapy (cervix)

Indication
Chemo-radiation for cervix cancers stages IB-IVA.

ICD-10 codes
Codes prefixed with C53

Regimen details

Day	Drug	Dose	Route
1	Cisplatin	40 mg/m² (max dose 70mg)	IV infusion

Cycle frequency
7 days

Number of cycles
6 cycles

Administration
Cisplatin is administered in 500mL sodium chloride 0.9% over 1 hour following the pre and post hydration protocol below.

Infusion Fluid & Additives	Volume	Infusion Time
Sodium Chloride 0.9%	1000mL	1 hour
Mannitol 20% **OR** Mannitol 10%	200mL 400mL	30 minutes 30 minutes
Ensure urine output > 100mL / hour prior to giving cisplatin. Give a single dose of furosemide 20mg iv if necessary.		
Cisplatin	500mL	1 hour
Sodium Chloride 0.9% + 2g $MgSO_4$ + 20mmol KCl	1000mL	2 hours
TOTAL	**2700mL or 2900mL**	**4 hours 30 minutes**

Patients with low magnesium levels (<0.7 mmol/L) should have an additional 2g magnesium sulphate added to the pre-hydration bag.

An accurate fluid balance record must be kept.

All patients must be advised to drink at least 2 litres of fluid over the following 24 hours.

Pre-medication
Pre-hydration as above.

Emetogenicity
This regimen has moderate emetogenic potential.

Additional supportive medication
If magnesium levels are consistently low, consider supplementation with oral magnesium. For example magnesium glycerophosphate [Note: unlicensed product] 24 mmol Mg^{2+} per day in divided doses or as per local magnesium replacement guidelines.

Extravasation
Cisplatin is an exfoliant (Group 4)

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC	14 days
U+E (including creatinine)	14 days
LFT	14 days
Magnesium	14 days

Investigations – pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	72 hours
U+E (including creatinine)	72 hours
LFT	72 hours
Magnesium	72 hours

Standard limits for administration to go ahead
If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	**Limit**
Neutrophils	≥1.5x 10^9/L
Platelets	≥100 x 10^9/L
Creatinine clearance (CrCl)	≥ 60 mL/min
Bilirubin	<1.5 x ULN
Magnesium	≥ 0.7 mmol/L

Dose modifications
- **Haematological toxicity**

Defer treatment for 1 week if neutrophils <1.5 x 10^9/L and/or platelets < 100 x 10^9/L.

If haemoglobin <11.5 g/dL a 2 unit blood transfusion should be arranged.

- **Renal impairment**

CrCl (mL/min)	**Cisplatin Dose**
≥60	100%
50-59	Discuss with consultant
<50	Omit

- **Hepatic impairment**

No dose reduction necessary.

- **Other toxicities**

Toxicity	Definition	Dose adjustment
Neurotoxicity	Grade 2	Discuss with consultant
	Grade 3-4	Discontinue
Ototoxicity	Grade 2	Discuss with consultant
	Grade 3-4	Discontinue

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Nephrotoxicity
Ototoxicity
Allergic reactions

- **Frequently occurring side effects**

Nausea/vomiting
Myelosuppression
Constipation
Peripheral neuropathy
Alopecia
Fatigue
Electrolyte disturbances
Taste disturbance

Significant drug interactions – for full details consult product literature/ reference texts

Allopurinol, colchicine, probenecid, sulfinpyrazone: increase serum uric acid concentration.
Cephalosporins, aminoglycosides, amphotericin B: increase nephrotoxic and ototoxic effects of cisplatin when administered simultaneously or 1-2 weeks after treatment with cisplatin.
Ciclosporin: excessive immunosuppression, with risk of lymphoproliferation.
Cyclizine, phenothiazines: may mask ototoxicity symptoms.
Furosemide, hydralazine, diazoxide, propranolol: intensify nephrotoxicity.
Oral anticoagulants: require an increased frequency of the INR monitoring.
Penicillamine: may diminish the effectiveness of cisplatin.
Phenytoin: reduced serum levels of phenytoin (due to reduced absorption and/or increased metabolism) can reduce epilepsy control. Monitor phenytoin levels.

Additional comments

Nil

References

- Rose, P.G. et al. Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer. NEJM 1999; 340: 1144-1153
- Summary of Product Characteristics Cisplatin (Hospira) accessed 17 Sept 2014 via www.medicines.org.uk
- Allwood M, Stanley A, Wright P, editors. The cytotoxics handbook. 4th ed. Radcliffe Medical Press. 2002.

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