Cisplatin and Radiotherapy (Gynae)

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

Chemo-radiation for vaginal cancers

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
Up to 5 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 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**
Haemoglobin	≥115g/L
Neutrophils	≥1.5x 10^9/L
Platelets	≥100 x 10^9/L
Creatinine clearance (CrCl)	≥ 60 mL/min
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 <115 g/L proceed with chemotherapy but a 2 unit blood transfusion should be arranged as soon as possible.

- **Renal impairment**

CrCl (mL/min)	Cisplatin dose
≥60	100%
50-59	75%
40-49	50%
20-40	Cisplatin contraindicated, consider carboplatin AUC2
<20	Not suitable for platinum treatment, 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
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- Allwood M, Stanley A, Wright P, editors. The cytotoxics handbook. 4th ed. Radcliffe Medical Press. 2002.
- Samant, R. et al. Primary vaginal cancer treated with concurrent chemoradiation using Cis-platinum. Int J Radiat Oncol Biol Phys 2007;69(3):746-750

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