Three Weekly Cisplatin and Radiotherapy

Indication
Chemo-radiation for head and neck cancers.

WHO performance status 0-1.

ICD-10 codes
Codes prefixed with C00-C13.

Regimen details

Day	Drug	Dose	Route
1	Cisplatin	100 mg/m²	IV infusion

Cycle frequency
21 days

Number of cycles
2- 3 cycles (i.e. on days 1 and 22 with a dose on day 43 if radiotherapy over 7 weeks).

Administration
Cisplatin is administered in 1000mL sodium chloride 0.9% over 2 hours 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	1000mL	2 hours
Sodium Chloride 0.9% + 2g $MgSO_4$ + 20mmol KCl	1000mL	2 hours
TOTAL	**3200mL or 3400mL**	**5 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 high emetogenic potential. An NK1 inhibitor is recommended.

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
Haemoglobin (Hb)	≥ 100g/L (If Hb< 115 g/L) a 2unit blood transfusion should be arranged)
Creatinine clearance (CrCl)*	≥ 60 mL/min
Bilirubin	<1.5 x ULN
Magnesium	≥ 0.7 mmol/L

*formal measurement of renal function is recommended prior to first dose.

Dose modifications
- **Haematological toxicity**

Neutrophils (x 10^9/L)		**Platelets** (x 10^9/L)	**Cisplatin dose**
≥1.5	and	≥100	100%
1.0-1.4	or	50-99	Delay 1 week (continue radiotherapy) If FBC recovers continue with 80% dose.
<1.0	or	<50	Delay 1 week (continue radiotherapy) If FBC recovers continue with 60% dose.

If Hb<115g/L a 2unit blood transfusion should be arranged. If Hb<100g/L delay treatment.

- **Renal impairment**

CrCl (mL/min)	**Cisplatin Dose**
≥60	100%
50-59	Discuss with consultant. Consider 80% dose.
<50	Omit. Consider switching to carboplatin AUC 5*

* if Cr Cl < 20mL/min carboplatin is contraindicated.

- **Hepatic impairment**

No dose reduction necessary.

- **Other toxicities**

Toxicity	**Definition**	**Dose adjustment**
Neurotoxicity	Grade 2	Discuss with consultant. Consider 80% dose.
	Grade 3-4	Discontinue cisplatin. Consider switching to carboplatin AUC 5
Ototoxicity	Grade 2	Discuss with consultant. Consider 80% dose.
	Grade 3-4	Discontinue cisplatin. Consider switching to carboplatin AUC 5

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
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

References

- Summary of Product Characteristics Cisplatin (Hospira) accessed 2 October 2019 via www.medicines.org.uk
- Mehanna, H et al. Radiotherapy plus cisplatin or cetuximab in low risk human papillomavirus positive oralpharyngeal cancer (DeESCALATE HPV): an open labelled randomised controlled phase 3 trial. Lancet 2019; 393: 51–60.

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