# HIGH DOSE TIP
# Cisplatin, Ifosfamide & Paclitaxel (Teratoma, Seminoma

Cumbria, Northumberland, Tyne & Wear Area Team

## DRUG ADMINISTRATION SCHEDULE

| Day | Drug | Dose | Route | Diluent | Rate |
|---|---|---|---|---|---|
| 0 | Dexamethasone | 20mg | **ORAL** | 12 hours & 6 hours before paclitaxel | |
| 1 | Ondansetron* | 8mg | Oral /Slow bolus/15 min infusion | | |
| 1 | Chlorphenamine | 10mg | IV | | Slow Bolus |
| 1 | Ranitidine | 50mg | IV | Diluted to at least 20mls NaCl 0.9% | 15 mins |
| **1** | **Paclitaxel** | **250mg/m$^2$** | **IV** | **500ml Sodium Chloride 0.9%** | **3 hours** |
| **2-5** (repeat on each day) | 20mmol Potassium and 10mmol Magnesium | 1000ml | IV | Sodium Chloride 0.9% | 4 hours |
| | **Cisplatin** | **25mg/m$^2$** | **IV** | **1000ml Sodium Chloride 0.9%** | **4 hours** |
| | **Ifosfamide** | **1500mg/m$^2$** | **IV** | Combined in same IV bag or infused together in separate bags. **1000 ml Sodium Chloride 0.18%, Glucose 4%** | **3 hours** |
| | **Mesna** | **1500mg/m$^2$** | | | |
| | **Mesna** | **900mg/m$^2$** | **IV** | **1000ml Sodium Chloride 0.9%** | **12 hours** |
| **6** | **Pegylated Filgrastim** | **6mg** | **SC** | | |

*Ondansetron IV must be infused over 15 minutes in patients over 65 years of age.

*Hydration schedules may be modified according to local agreement.*

Text in blue highlights the differences between the higher and lower dose schedules.

## CYCLE LENGTH AND NUMBER OF DAYS

21 Day cycle for 4 to 6 cycles.

## APPROVED INDICATIONS

- Teratoma: Second line treatment of metastatic teratoma

## EXCLUSION CRITERIA

- Inadequate haematological function
- Inadequate renal function (GFR < 40ml/min)

## RECOMMENDED TAKE HOME MEDICATION

**Start:**

- Ondansetron 8mg twice daily orally, starting approximately 12 hours after IV dose on day 1 and continue until end of day 7.
- Dexamethasone 4mg twice daily orally, after IV dose on day 1 and continue until end of day 6.
- Metoclopramide 10mg Three Times a Day as required.

## INVESTIGATIONS / MONITORING REQUIRED

**Prior to first cycle:** FBC, U&Es (Calculated CrCl, or measured GFR), LFTs (including LDH), Mg & Ca, Plumonary Function Test if clinical concern. Tumour markers (AFP / β-HCG).

**Prior to each cycle:** U&Es, LFTs (including LDH), Mg, FBC. Tumour markers, CrCl.

## ASSESSMENT OF RESPONSE

Radiologically (half way through treatment) and tumour markers (each cycle).

## REVIEW BY CLINICIAN

Prior to each cycle, unless being reviewed by a Nurse Specialist or Pharmacist under a locally agreed framework.

## NURSE / PHARMACIST LED REVIEW

As per locally agreed framework.

## ADMINISTRATION NOTES

- Treatment delays should be avoided as this may reduce the effectiveness of treatment
- Aminoglycoside anti-biotics should usually be avoided due to risk of additional renal toxicity which may occur with cisplatin.
- Paclitaxel must be administered via a non-PVC administration set
- There is a risk of infusion reactions with paclitaxel. This is commonly with the first two cycles and often within the first few minutes of starting chemotherapy.
- May not need to stop treatment for minor hypersensitivity e.g. reactions, flushing, localised rash. Must be stopped for major reactions, e.g. hypotension, dyspnoea, angioedema or generalised urticaria.
- If patient has hypersensitivity reaction follow manufacturers re-challenge guidelines before continuing with treatment.
- Units administering Paclitaxel must have facilities available for the treatment of anaphylaxis and resuscitation.
- Blood Pressure & Pulse should be monitored regularly (eg every 30 minutes) during pacliataxel infusion
- Ifosfamide can cause haemorrhagic cystitis – patients must receive Mesna prophylaxis with the ifosfamide infusion. In the event of micro or macroscopic haematuria the dose of mesna should be increased.
- Ifosfamide can cause encephalopathy. If this occurs the ifsofamide infusion should be stopped. Consider treating severe cases with methylene blue (50mg IV 6 times daily, or 50mg orally 4 times daily). Methylene blue can also be used prophylactically to allow ifosfamide to be restarted.

## TOXICITIES

Common: Allopecia, Emesis, Myelosuppression,
Less Common: Tinnitus, Nephrotoxicity, Peripheral Neuropathy

## DOSE MODIFICATION / TREATMENT DELAYS

### Neurotoxicity

| Grade | Cisplatin Dose |
|---|---|
| 1 | 100% |
| 2 | 50% |
| 3 or 4 | Omit |

**Haematological Toxicity:**
Delay treatment if ANC < 1.0 x $10^9$ cells/l or PLT < 100 x $10^9$ cells/l.

**Renal Function:**
Cisplatin is renally excreted, dose modification of cisplatin should be considered when CrCl is less that 60ml/min..

| CrCl (or GFR) | Cisplatin |
|---|---|
| > 60ml/min | 100% |
| 51 – 60ml/min | 75% |
| 40 - 50ml/min | 50% |
| 40 - 30 ml/min | Contra-indicated |
| 10 - 30ml/min | Contra-indicated |
| < 10ml/min | Contra-indicated |

**Hepatic Function:**
Paclitaxel is hepatically cleared and impairment may result in significant haematological toxicity. Clear guidance about dose modification is not available, however, if Bilirubin is > 1.25 x ULN dose modification is probably required, with larger reductions being needed when Bilirubin is > 2 x ULN and use of paclitaxel should be considered contra-indicated when Bilirubin is > 5 x ULN.

## TREATMENT LOCATION
Only suitable for administration as an in-patient regimen at a Cancer Centre.

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## Document Control

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| | 1.1 | Protocol reviewed and reissued, Antiemetic advice updated | |
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