Cisplatin/ Oral Etoposide (Rotterdam regimen)

NHS Northern Cancer Alliance

DRUG ADMINISTRATION SCHEDULE

Day	Drug	Daily Dose	Route	Diluent & Rate
Days 1, 8 & 15	Sodium Chloride 0.9%	250 ml	IV Infusion	Fast Running
	Mannitol 20% ***or*** Furosemide	100mls ***or*** 20mg	IV Infusion ***or*** IV bolus	100mls over 30 minutes ***or*** Via saline drip
	Mg SO4 KCl	10mmol 20mmol	IV Infusion	1000ml 0.9% Sodium Chloride over 2 hours
	Dexamethasone	8mg	Oral	
	Ondansetron*	8mg	Oral/Slow bolus/15 min infusion	
	CISplatin	**50 mg/m^2**	**IV infusion**	**1000ml 0.9% Sodium Chloride over 2 hours**
	Mg SO4 KCl	10mmol 20mmol	IV Infusion	1000ml 0.9% Sodium Chloride over 2 hours
Days 1 to 15	**Etoposide**	**50mg ONCE Daily**	**Oral**	**-**

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

Either Mannitol 20% or Furosemide can be used to ensure adequate urine flow

NUMBER OF DAYS PER CYCLE

28-day cycle for 2 Cycles (6 doses of cisplatin)

Maintenance post 6th Cisplatin: Etoposide 50 mg/m^2 daily for 21 days of a 28-day cycle. In practice as oral etoposide capsules are only available in 50mg or 100mg, most patients will be given 100mg daily

APPROVED INDICATIONS

2nd, 3rd line: Ovarian, Endometrial, Cervical, Ewing's sarcoma.
Relapsed ovarian cancer

ELIGIBILITY CRITERIA

Adequate cardiac and renal function (GFR over 60 mL/min)

PREMEDICATION

Adequate hydration and urinary flow is essential when administering cisplatin. Patients should be weighed (with bladder empty) prior to commencing treatment and use 20 mg of IV furosemide or 100ml mannitol 20% as a diuretic given routinely if there is no contraindication. Patient should be re-weighed at the end of cisplatin (with empty bladder) and consideration given to administering a further dose of furosemide if weight gain is more than 1.5 Kg. Patients must be encouraged to drink 1 to 2 litres of water over next 24 hours post treatment

RECOMMENDED TAKE HOME MEDICATION

Ondansetron 8mg twice daily for 2 to 3 days
Dexamethasone 4mg twice daily for 1 to 3 days
Metoclopramide 10mg three times daily as required* see CINV policy for precautions
Suggested antiemetic regimen - may vary with local practice. See CINV policy for more details

INVESTIGATIONS / MONITORING REQUIRED

Pre-treatment

FBC, U&Es and LFTs. Check renal function before commencing platinum. Use EDTA or Wright to calculate baseline GFR.

Prior to each cycle

FBC, U&Es, LFTs and calculation of GFR using Wright formulae.

ASSESSMENT OF RESPONSE

Metastatic: Tumour size and patient symptomatic response

REVIEW BY CLINICIAN

To be reviewed by either a Nurse, Pharmacist or Clinician before every cycle.

NURSE / PHARMACIST LED REVIEW

On cycles where not seen by clinician.

ADMINISTRATION NOTES

Check renal function before commencing platinum. Use EDTA or Wright to calculate GFR. GFR must be above 60 mL/min for cisplatin-based treatment. If GFR < 60 mL/min discuss with an Oncology Specialist.

If the Cockcroft & Gault calculated clearance alters by >20%, an EDTA clearance should be repeated and modification of the chemotherapy dose may be required, Discuss with an Oncology Specialist.

EXTRAVASATION *See NCA/Local Policy*

TOXICITIES

Oral Etoposide is not very well tolerated in this group of patients as most will have either advanced disease or have been heavily pre-treated with chemotherapy.

- Rare - allergic or anaphylactic reactions. Nausea & Vomiting
- Mucositis
- Constipation
- Alopecia
- Bone Marrow Depression; anaemia, neutropenia, thrombocytopenia
- Nephrotoxicity, monitor U&Es
- Alteration in LFTs (infrequent and transient)
- Leukaemic transformation
- Neurotoxicity (ototoxicity)
- Hypotension and bradycardia
- Peripheral neuropathy
- Myalgia

DOSE MODIFICATION / TREATMENT DELAYS

Haematological Toxicity:

- Proceed if neutrophil count > 1.5, WCC > 3.0, PLT >100, unless directed by an oncology specialist.

- If ANC, PLT or WCC still below required levels for treatment at after one-week delay, delay treatment again and patient will need assessed and chemotherapy dose reduction by Oncologist
- If Hb < 10 and patient symptomatic will need blood transfusion but may proceed with chemotherapy as planned if performance status (PS) stable.

Non-Haematological Toxicity:
If PS deteriorates to 3 or 4 and on assessment patient is more symptomatic withhold treatment and discuss with Oncologist

Cisplatin

- Baseline EDTA required. GFR prior to treatment should be > 60mL/min
- Serum creatinine should be checked before each cycle of treatment. If there is a > 25% increase compared to the baseline, then the EDTA must be repeated.
- If renal function deteriorates the Cisplatin dose can be adjusted as follows:

GFR (EDTA or measured Creatinine Clearance)	Cisplatin Dose
≥ 60 mL/min	Full dose
40 - 60 mL/min	Consider reducing to same cisplatin dose in mg as value of GFR in mL/min
< 40 mL/min	Omit cisplatin. Consider substituting for carboplatin

Conversely if a patient has a GFR < 60mL/min initially and there is improvement in serum creatinine the GFR should be rechecked with an EDTA clearance.

Patients with functional hearing loss should have cisplatin omitted. Carboplatin AUC 3-5 can be substituted but must be authorised by the SpR/Consultant. The change & reason must be clearly documented in the patient's clinical notes.

Etoposide

At decreased creatinine clearance of 15 to 50 mL/min a dose reduction of etoposide by 25% is recommended.

TREATMENT LOCATION
Can be given at Cancer Centre

REFERENCE

1. Van der Burg et al. Weekly cisplatin and daily oral etoposide is highly effective in platinum pretreated ovarian cancer. *British Journal of Cancer* (2002) 86, 19–25

Document Control

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Summary of Changes	1.1	Reformatted from old NCN/CCA versions	
	1.2	Protocol reviewed. Typing errors corrected.	
	1.3	Protocol reviewed and approval dates updated	
	1.4	Updated against Chemocare parameters, formatting tidied, hydration advice updated	