**Cisplatin/ Oral Etoposide (Rotterdam regimen)**

### DRUG ADMINISTRATION SCHEDULE

<table>
<thead>
<tr>
<th>Day</th>
<th>Drug</th>
<th>Daily Dose</th>
<th>Route</th>
<th>Diluent &amp; Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days 1, 8 &amp; 15</td>
<td>Sodium Chloride 0.9%</td>
<td>250 ml</td>
<td>IV Infusion</td>
<td>Fast Running</td>
</tr>
<tr>
<td></td>
<td>Mannitol 20% or Furosemide</td>
<td>100mls or 20mg</td>
<td>IV Infusion or IV bolus</td>
<td>100mls over 30 minutes or Via saline drip</td>
</tr>
<tr>
<td></td>
<td>Mg SO4 KCl</td>
<td>10mmol 20mmol</td>
<td>IV Infusion</td>
<td>1000ml 0.9% Sodium Chloride over 2 hours</td>
</tr>
<tr>
<td></td>
<td>Dexamethasone</td>
<td>8mg</td>
<td>Oral</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ondansetron*</td>
<td>8mg</td>
<td>Oral/Slow bolus/15 min infusion</td>
<td></td>
</tr>
<tr>
<td>Days 1 to 15</td>
<td>CISplatin</td>
<td>50 mg/m²</td>
<td>IV infusion</td>
<td>1000ml 0.9% Sodium Chloride over 2 hours</td>
</tr>
<tr>
<td></td>
<td>Mg SO4 KCl</td>
<td>10mmol 20mmol</td>
<td>IV Infusion</td>
<td>1000ml 0.9% Sodium Chloride over 2 hours</td>
</tr>
<tr>
<td></td>
<td>Etoposide ONCE Daily</td>
<td>50mg</td>
<td>Oral</td>
<td>-</td>
</tr>
</tbody>
</table>

*Ondansetron IV must be infused over 15 minutes 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/m² 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.
Cisplatin/ Oral Etoposide (Rotterdam regimen)

- 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:

<table>
<thead>
<tr>
<th>GFR (EDTA or measured Creatinine Clearance)</th>
<th>Cisplatin Dose</th>
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<tbody>
<tr>
<td>≥ 60 mL/min</td>
<td>Full dose</td>
</tr>
<tr>
<td>40 - 60 mL/min</td>
<td>Consider reducing to same cisplatin dose in mg as value of GFR in mL/min</td>
</tr>
<tr>
<td>&lt; 40 mL/min</td>
<td>Omit cisplatin. Consider substituting for carboplatin</td>
</tr>
</tbody>
</table>

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


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### Document Control

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<thead>
<tr>
<th>Document Title:</th>
<th>Cisplatin/ Oral Etoposide (Rotterdam regimen)</th>
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<td>Document No:</td>
<td>CRP09 GY005</td>
</tr>
<tr>
<td>Reviewer:</td>
<td>Chris Beck, Cancer Alliance pharmacist</td>
</tr>
<tr>
<td>Approved by:</td>
<td>Steve Williamson, Consultant Pharmacist, Northern Cancer Alliance</td>
</tr>
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<td>Current Version:</td>
<td>1.4</td>
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<td>Date Approved:</td>
<td>22/08/2018</td>
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<td>Due for Review:</td>
<td>22/08/2021</td>
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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