

Chemotherapy Protocol
GYNAECOLOGICAL CANCER
CISPLATIN-ETOPOSIDE
(oral)

Regimen

- Uterine-Cisplatin-Etoposide PO

Indication

- Treatment of partially platinum-sensitive or platinum-refractory relapsed ovarian cancer.
- Small cell gynaecological cancers including those affecting the cervix, endometrium and ovaries.
- WHO performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Cisplatin	Neuropathy, nephrotoxicity, ototoxicity
Etoposide	Alopecia, hyperbilirubineamia

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

Drugs

- FBC, U&Es and LFTs prior to days 1, 8, 15 of treatment
- EDTA or calculated creatinine clearance prior to day 1 of each cycle
- CA125 prior to day 1 of each cycle
- Consider formal audiology testing

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

Haematological

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL.

Prior to Cycle 1 the following criteria must be met;

Criteria	Eligible Level
Neutrophil	equal to or more than $1 \times 10^9/L$
Platelets	equal to or more than $100 \times 10^9/L$

Day 1 - Dose modifications

Neutrophils ($\times 10^9/L$)	Dose Modifications (cisplatin and etoposide)
1 or greater	100%
less than 1	Delay treatment for 7 days. If resolved to $1 \times 10^9/L$ or greater after 7 days continue at the full dose
Platelets ($\times 10^9/L$)	Dose Modifications (cisplatin and etoposide)
100 or greater	100%
less than 100	Delay treatment for 7 days. If resolved to $100 \times 10^9/L$ or greater after 7 days continue at the full dose

Day 8 and 15 - Dose modifications

Neutrophils ($\times 10^9/L$)	Dose Modifications (cisplatin and etoposide)
1 or greater	100%
less than 1	Delay the cisplatin and stop the etoposide
Platelets ($\times 10^9/L$)	Dose Modifications (cisplatin and etoposide)
50 or greater	100%
less than 50	Delay the cisplatin and stop the etoposide

Hepatic Impairment

Drug	Bilirubin (µmol/L)		AST/ALT units	Dose (% of original dose)
Cisplatin	N/A		N/A	No dose adjustment needed
Etoposide	26-51	or	60-180	Consider reducing course length
	51 or greater	or	180 or greater	Clinical decision

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Cisplatin	60 or greater	100%
	45-59	75%
	less than 45	Consider alternative
Etoposide	50 or greater	100%
	15-50	75%
	less than 15	50%

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

For all other non-haematological NCI-CTC grade 3 and above toxicities delay treatment until the adverse effect has resolved to NCI-CTC grade 1 or below. The dose of the causative agent should then be reduced to 75% of the original dose or discontinued as appropriate.

Regimen

28 day cycle for 2 cycles

Drug	Dose	Days	Administration
Cisplatin	50mg/m ²	1, 8, 15	Intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride at a rate of 1mg/min cisplatin (minimum 120 minutes)
Etoposide	50mg (flat dose)	1-14 incl.	Oral

Followed by:

28 day cycle for 6 to 9 cycles (six cycles will be set in Aria)

Drug	Dose	Days	Administration
Etoposide	50mg (flat dose)	1-21 incl.	Oral

[Dose Information](#)

- Cisplatin will be dose banded according to the CSCCN agreed bands.

[Administration Information](#)

Extravasation

- Cisplatin – exfoliant

Other

- Etoposide to be taken an hour before food or on an empty stomach

[Additional Therapy](#)

- Antiemetics cycle one and two

15-30 minutes prior to chemotherapy cycle one and two only

- aprepitant 125mg oral
- dexamethasone 4mg oral or intravenous
- ondansetron 8mg oral or intravenous

As take home medication – Day 1, 8, 15 cycle one and two

- aprepitant 80mg oral once a day for 2 days (Days 2 & 3)
- dexamethasone 4mg oral once a day for 3 days
- metoclopramide 10mg oral three times a day as required (Cycle 1 only)
- ondansetron 8mg oral twice a day for 3 days

- Cisplatin pre and post hydration as follows;

Pre

Furosemide 40mg oral or intravenous

1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes

Post

1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol

magnesium sulphate over 60 minutes

Patients should be advised to drink at least 3 litres of fluid in the 24 hours after administration of cisplatin.

- Gastric protection with a proton pump inhibitor or a H₂ antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

[Additional Information](#)

- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to etoposide.

[Coding \(OPCS 14-15\)](#)

- Procurement – X70.2
- Delivery – X72.1

[References](#)

1. van der Burg M, de Wit R, van Putten W et al. Weekly cisplatin and daily oral etoposide is highly effective in platinum pretreated ovarian cancer. Br J Cancer 2002; 86 (1): 19–25.
2. Meyer T, Nelstrop AE, Mahmoudi M et al. Weekly cisplatin and oral etoposide as treatment for relapsed epithelial ovarian cancer. Ann Oncol. 2001; 12 (12): 1705-9.

REGIMEN SUMMARY

Cisplatin-Etoposide PO

Cycles One and Two

Day 1, 8, 15

1. Aprepitant 125mg oral
2. Dexamethasone 4mg oral or intravenous
3. Ondansetron 8mg oral or intravenous
4. Furosemide 40mg oral or intravenous
5. Sodium chloride 0.9% 1000ml with magnesium sulphate 16mmol and potassium chloride 20mmol intravenous infusion over 60 minutes
6. Cisplatin 50mg/m² in 1000ml sodium chloride 0.9% with 20mmol potassium chloride intravenous infusion at a rate of 1mg/min cisplatin (minimum 120 minutes)
7. Sodium chloride 0.9% 1000ml with magnesium sulphate 16mmol and potassium chloride 20mmol intravenous infusion over 60 minutes

Take Home Medicines

8. Etoposide 50mg oral once a day for 14 days
9. Aprepitant 80mg oral once a day for 2 days starting the day after intravenous chemotherapy
Administration Instructions
Please supply sufficient quantities for days 1, 8, 15 of the cycle
10. Dexamethasone 4mg oral once a day for 3 days starting the day after intravenous chemotherapy
Administration Instructions
Please supply sufficient quantities for days 1, 8, 15 of the cycle
11. Metoclopramide 10mg oral three times a day when required for nausea
Administration Instructions
Please supply 60 tablets or appropriate equivalent
12. Ondansetron 8mg oral twice a day for 3 days starting on the evening of intravenous chemotherapy
Administration Instructions
Please supply sufficient quantities for days 1, 8, 15 of the cycle

Cycle Three, Four, Five, Six, Seven and Eight

Day 1 – Take Home Medicines

13. Etoposide 50mg oral once a day for 21 days

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	March 2014	Name changed to add PO "Intravenous bolus" changed to bolus Daily changed to once a day Metoclopramide dose changed from 10-20mg to 10mg OPCS updated Disclaimer updated	Dr Deborah Wright Pharmacist	Donna Kimber Pharmacy Technician
1	May 2013	None	Rebecca Wills Pharmacist Dr Deborah Wright Pharmacist	Dr Clare Green Consultant Medical Oncologist Dr Cheng Yeoh Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
 NHS Isle of Wight
 Portsmouth Hospitals NHS Trust
 Salisbury Hospital NHS Foundation Trust
 University Hospital Southampton NHS Foundation Trust
 Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.