Chemotherapy Protocol

GYNAECOLOGICAL CANCER

CYCLOPHOSPHAMIDE ORAL

Regimen

- Ovary – Cyclophosphamide Oral

Indication

- Relapsed/refractory ovarian cancer in patients unsuitable for other treatments
- Palliative
- Performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Cyclophosphamide	Dysuria, haemorrragic cystitis (rare), taste disturbances

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

Monitoring

Drugs

- FBC, LFT's and U&E's prior to day one of treatment

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.

Day 1

Neutrophils ($x10^9$/L)	Dose Modifications
1 or greater	100%
less than 1	Withhold the cyclophosphamide until recovery to $1x10^9$/L or greater. If recovered to this level within 7 days resume treatment at full the dose. If not recovered at this point delay until recovery then continue with 50mg on alternate days or discontinue as appropriate.
Platelets ($x10^9$/L)	**Dose Modifications**
75 or greater	100%
less than 75	Withhold the cyclophosphamide until recovery to $75x10^9$/L or greater. If recovered to this level within 7 days resume treatment at full dose. If not recovered at this point delay until recovery then continue with 50mg on alternate days or discontinue as appropriate.

Hepatic Impairment

Drug	Bilirubin (µmol/L)		AST/ALT units	Dose (% of original dose)
Cyclophosphamide	20 or greater	or	2-3xULN	Clinical decision. Evidence that exposure to active metabolites may not be increased, suggesting dose reduction may not be necessary.

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Cyclophosphamide	20 or greater	100%
	10-20	Consider 50mg on alternate days
	less than 10	omit

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. Consider giving 50mg on alternate days or discontinue as appropriate.

Regimen

28 day cycle for 6 cycles

Drug	Dose	Days	Administration
Cyclophosphamide	50mg (flat dose)	1-28 incl.	Oral

Administration Information

- Cyclophosphamide to be taken with plenty of water swallowed whole, not chewed

Additional Therapy

Antiemetics

- As take home medication
    - metoclopramide 10mg oral three times a day when required
- Gastric protection with a proton pump inhibitor or a H_2 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 oral cyclophosphamide.

Coding (OPCS 4.6)

- Procurement – X70.1
- Delivery – X73.1

References

1. Watanabe Y, Etoh T, Koike E et al. Feasibility study of oral cyclophosphamide salvage therapy for the treatment of heavily pre-treated patients with recurrent epithelial ovarian cancer. Int J Clin Oncol 2010; 16 (5): 468-471.
2. Garcia AA, Hirte H, Fleming G, et al.: Phase II clinical trial of bevacizumab and low-dose metronomic oral cyclophosphamide in recurrent ovarian cancer: a trial of the California, Chicago, and Princess Margaret Hospital phase II consortia. J Clin Oncol 26 (1): 76-82, 2008.

REGIMEN SUMMARY

Cyclophosphamide PO

Day 1

1. Cyclophosphamide 50mg (flat dose) oral once a day for 28 days
2. Metoclopramide 10mg oral three times a day when required

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	April 2014	Metoclopramide dose changed Disclaimer updated	Dr Deborah Wright Pharmacist	Donna Kimber Pharmacy Technician
1	May 2013	None	Rebecca Wills Pharmacist Dr Deborah Wright Pharmacist	Dr Deborah Wright 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.