

## Chemotherapy Protocol

### LYMPHOMA

#### CYCLOPHOSPHAMIDE-ETOPOSIDE-PREDNISOLONE-VINCRISTINE

#### (CEOP)

##### Regimen

- Lymphoma – CEOP-Cyclophosphamide-Etoposide-Prednisolone-Vincristine

##### Indication

- Non-Hodgkin's Lymphoma where the use of an anthracycline based regimen is contra-indicated
- T-cell non-Hodgkin's Lymphoma

##### Toxicity

Drug	Adverse Effect
Cyclophosphamide	Dysuria, haemorrhagic cystitis (rare), taste disturbances
Etoposide	Hypotension on rapid infusion, alopecia, hyperbilirubinaemia
Vincristine	Peripheral neuropathy, constipation, jaw pain
Prednisolone	Weight gain, gastro-intestinal disturbances, hyperglycaemia, CNS disturbances, cushingoid changes, glucose intolerance

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

##### Monitoring

##### *Drugs*

- FBC, LFTs and U&Es, prior to day one of treatment
- Albumin prior to each cycle

##### Dose Modifications

The dose modifications listed are for haematological, liver and renal function and some 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

Dose modifications for haematological toxicity in the table below are for general guidance only. Always refer to the responsible consultant as any dose reductions or delays will be dependent on clinical circumstances and treatment intent. Low counts can be a consequence of bone marrow infiltration as well as drug toxicity.

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

Dose modifications based on haematological parameters apply to cyclophosphamide and etoposide only

Neutrophils ( $\times 10^9/L$ )	Dose Modifications (cyclophosphamide and etoposide)
1 or greater	100%
0.5 - 0.9	<p>1<sup>st</sup> Occurrence If the intent is curative and growth factor prophylaxis has <u>not</u> been previously given administer 100% of the dose plus prophylactic growth factors.</p> <p>Alternatively delay until the neutrophils are <math>1 \times 10^9/L</math> or above and then give 75% of the original dose</p> <p>2<sup>nd</sup> Occurrence Delay until neutrophils are <math>1 \times 10^9/L</math> or above and then give 50% of the original dose plus prophylactic growth factors</p>
less than 0.5 or febrile neutropenia	<p>1<sup>st</sup> Occurrence Delay until the neutrophils are <math>1 \times 10^9/L</math> or above and then give 75% of the original dose plus prophylactic growth factors</p> <p>2<sup>nd</sup> Occurrence Delay until the neutrophils are <math>1 \times 10^9/L</math> or above and then give 50% of the original dose plus prophylactic growth factors</p>
Platelets ( $\times 10^9/L$ )	Dose Modifications (Cyclophosphamide and Etoposide)
75 or above	100%
50 – 74	<p>1<sup>st</sup> Occurrence Give 75% of the dose</p> <p>2<sup>nd</sup> Occurrence Give 50% of the dose</p>
Less than 50 or signs of active haemorrhage	<p>1<sup>st</sup> Occurrence Delay until the platelets are 75 or above then give 75% of the original dose</p> <p>2<sup>nd</sup> Occurrence Delay until the platelets are 75 or above then give 50% of the original dose</p>

### Hepatic Impairment

Please note that the approach may be different where abnormal liver function tests are due to disease involvement.

Drug	Bilirubin ( $\mu$ mol/L)		AST/ALT (units/L)	Dose (% of original dose)
Cyclophosphamide	Evidence suggests dose reduction not necessary.			
Etoposide	*30-51	or	60-180	Consider dose reducing to 50%
	more than 51	or	More than 180	Clinical decision
Vincristine	*30-51	or	60-180	50%
	more than 51	and	normal	50%
	more than 51	and	more than 180	omit

\* The lower limit reflects local practice and may differ from published sources.

### Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Cyclophosphamide**	more than 20	100%
	10-20	75%
	less than 10	50%
Etoposide	more than 50	100%
	15-50	75%
	Less than 15	50%
Vincristine	N/A	No dose adjustment needed

\*\*Consider mesna in patients with pre-existing bladder disorders. Give an oral dose of 40% of the cyclophosphamide dose (rounded upwards to the nearest 400mg) at 0, 2 and 6 hours after the administration of the cyclophosphamide.

## 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.

## Etoposide

Where significant reductions in albumin levels occur consider reducing the dose of etoposide.

## Vincristine

Reduce the vincristine dose to 1mg if a NCI-CTC grade 2 motor or grade 3 sensory neurological toxicity occurs. For higher toxicity grades or if toxicity increases despite dose reduction stop the vincristine.

## Regimen

### 21 day cycle for 6 cycles

Drug	Dose	Days	Administration
Cyclophosphamide	750mg/m <sup>2</sup>	1	Intravenous bolus over 10 minutes
Etoposide	150mg/m <sup>2</sup>	1	Intravenous infusion in 1000ml sodium chloride 0.9% over 60 minutes
Vincristine	1.4mg/m <sup>2</sup> (max 2mg)	1	Intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes
Etoposide	100mg/m <sup>2</sup>	2 and 3	Oral
Prednisolone	100mg	1, 2, 3, 4 and 5	Oral

Consider initial dose reduction in patients over 70 years of age. Doses may be escalated up to full dose on subsequent cycles according to tolerability.

## Dose Information

- Cyclophosphamide will be dose banded according to the CSCCN agreed bands
- Etoposide (intravenous) will be dose banded according to the CSCCN agreed bands
- Etoposide (oral) is available as 50mg and 100mg capsules. All doses will be rounded to the nearest 50mg (up if halfway).
- Vincristine will be rounded to the nearest 0.1mg (up if halfway)
- The maximum dose of vincristine is 2mg

## Administration Information

### *Extravasation*

- Cyclophosphamide – neutral
- Etoposide – irritant
- Vincristine - vesicant

### *Other*

- Prednisolone should be taken in the morning with or after food.
- Etoposide (oral) should be taken an hour before food or on an empty stomach

## Additional Therapy

- Antiemetics  
15-30 minutes prior to chemotherapy
  - ondansetron 8mg oral or intravenousAs take home medication
  - metoclopramide 10mg three times a day when required oral
  - ondansetron 8mg twice a day for 3 days oral
- Allopurinol 300mg once a day oral for the first cycle only
- Consider anti-infective prophylaxis in high risk patients, including:
  - aciclovir 400mg twice a day oral
  - co-trimoxazole 960mg once a day on Monday, Wednesday and Friday only oral
- Mouthwashes according to local or national policy on the treatment of mucositis
- 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 Agency alert NPSA/2008/RRR001 must be followed when prescribing, dispensing or administering oral chemotherapy.
- It must be made clear to all staff, including those in the community, that this is a short course of oral chemotherapy that must not be continued.
- Patients should be assessed for suitability for oral chemotherapy prior to starting treatment.
- The National Patient Safety Agency report NPSA/2008/RRR04 must be followed in relation to intravenous administration of vinca alkaloids.

### [Coding](#)

- Procurement – X70.8
- Delivery – X72.9

## REGIMEN SUMMARY

### CEOP-Cyclophosphamide-Etoposide-Prednisolone-Vincristine

#### Cycle 1

1. Ondansetron 8mg oral or intravenous injection
2. Prednisolone 100mg oral
3. Vincristine 1.4mg/m<sup>2</sup> (max 2mg) intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes
4. Etoposide 150mg/m<sup>2</sup> intravenous infusion in 1000ml sodium chloride 0.9% over 60 minutes
5. Cyclophosphamide 750mg/m<sup>2</sup> intravenous bolus over 10 minutes

#### Take Home Medicines

6. Etoposide 100mg/m<sup>2</sup> once a day for 2 days oral (starting on day 2)
7. Prednisolone 100mg once a day for 4 days oral (starting on day 2)
8. Allopurinol 300mg once a day oral for 21 days
9. Metoclopramide 10mg three times a day when required oral
10. Ondansetron 8mg twice a day for 3 days oral starting on the evening of day one of treatment

#### Cycles 2, 3, 4, 5 and 6

1. Ondansetron 8mg oral or intravenous injection
2. Prednisolone 100mg oral
3. Vincristine 1.4mg/m<sup>2</sup> (max 2mg) intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes
4. Etoposide 150mg/m<sup>2</sup> intravenous infusion in 1000ml sodium chloride 0.9% over 60 minutes
5. Cyclophosphamide 750mg/m<sup>2</sup> intravenous bolus over 10 minutes

### **Take Home Medicines**

6. Etoposide 100mg/m<sup>2</sup> once a day for 2 days oral (starting on day 2)
7. Prednisolone 100mg once a day for 4 days oral (starting on day 2)
8. Metoclopramide 10mg three times a day when required oral
9. Ondansetron 8mg twice a day for 3 days oral starting on the evening of day one of treatment



## DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.2	Jan 2015	Header changed Toxicities removed Hepatic & renal tables updated Metoclopramide dose changed to 10mg Bolos removed from intravenous bolus throughout text Mucositis recommendation changed Disclaimer added Document control reordered	Donna Kimber Pharmacy Technician	Rebecca Wills Pharmacist
1.1	July 2012	"In patients over 70 years of age consider using vincristine 1mg. Where appropriate dose reduction of other agents may be considered at cycle one" changed to "Consider initial dose reduction in patients over 70 years of age."	Rebecca Wills Pharmacist	Dr Debbie Wright Pharmacist
1	April 2012	None	Rebecca Wills Pharmacist  Dr Debbie Wright Pharmacist	Dr Andrew Davies Consultant Medical Oncologist  Dr Alison Milne Consultant Haematologist

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 Hospitals 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.