

## Chemotherapy Protocol

### LYMPHOMA

#### CHLORAMBUCIL-DOXORUBICIN-ETOPOSIDE-PREDNISOLONE-PROCARBAZINE-VINBLASTINE-VINCRIStINE

#### (ChIVPP-EVA)

##### Regimen

- Lymphoma – ChIVPP-EVA-Chlorambucil-Doxorubicin-Etoposide-Prednisolone-Procarbazine-Vinblastine-Vincristine

##### Indication

- Hodgkin's Lymphoma

##### Toxicity

Drug	Adverse Effect
Chlorambucil	Gastro-intestinal disturbance
Doxorubicin	Cardiomyopathy, alopecia, urinary discolouration (red)
Etoposide	Hypotension on rapid infusion, hyperbilirubinaemia
Prednisolone	Weight gain, gastro-intestinal disturbances, hyperglycaemia, CNS disturbances, cushingoid changes, glucose intolerance
Procarbazine	Insomnia, ataxia, hallucinations, headache
Vinblastine	Peripheral neuropathy, constipation, jaw pain, ileus
Vincristine	Peripheral neuropathy, constipation, jaw pain, ileus

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

Patients diagnosed with Hodgkin's Lymphoma carry a lifelong risk of transfusion-associated graft versus host disease (TA-GVHD). Where blood products are required these patients must receive only irradiated blood products for life. Local blood transfusion departments must be notified as soon as a diagnosis is made and the patient must be issued with an alert card to carry with them at all times.

##### Monitoring

##### Drugs

- FBC, LFTs and U&Es prior to day one and eight of treatment

## Dose Modifications

The dose modifications listed are for haematological, liver and renal function and limited drug specific toxicities. 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. **Irradiated blood products must be used in Hodgkin's Lymphoma patients.**

Treatment will proceed if the neutrophils are greater than or equal to  $1 \times 10^9/L$  and the platelet count is greater than or equal to  $100 \times 10^9/L$ . For values lower than these, treatment should be delayed by 7 or 14 days to allow full haematologic recovery. Growth factors are not normally required.

## Hepatic Impairment

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

Drug	Bilirubin (μmol/L)		AST/ALT (units/L)	Dose (% of original dose)
Chlorambucil				Dose reduce in severe hepatic impairment
Doxorubicin	less than *30	and	2-3xULN	75%
	*30-50	and/or	More than 3xULN	50%
	51-85		N/A	25%
	more than 85		N/A	omit
Etoposide	30-51	or	60-180	Consider dose reducing to 50%
	more than 51	or	more than 180	Clinical decision
Procarbazine	more than 50			Consider dose reduction
	more than 85	or	more than 180	Omit
Vinblastine	*30-51	or	60-180	50%
	more than 51	and	normal	50%
	more than 51	and	more than 180	Omit
Vincristine	*30-51	or	60-180	50%
	more than 51	and	normal	50%
	more than 51	and	more than 180	omit

\* Limits reflect local practice and may vary from published sources

## Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Chlorambucil		No dose adjustment needed
Doxorubicin	less than 10	Consider dose reduction in severe renal failure
Etoposide	more than 50	100%
	15-50	75%
	less than 15	50%
Procarbazine	more than 177 $\mu\text{mol/L}$	50%
	less than 10	Not recommended
Vinblastine	N/A	No dose adjustment needed
Vincristine	N/A	No dose adjustment needed

## 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.

## Doxorubicin

Discontinue doxorubicin if cardiac failure develops

## Etoposide

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

## Vinblastine

Reduce the vinblastine dose to  $3\text{mg/m}^2$  if NCI-CTC grade 2 motor or a NCI-CTC grade 3 sensory neurological toxicity occurs. For higher toxicity grades or if toxicity increases despite dose reduction stop the vinblastine.

## Vincristine

Reduce the vincristine dose to 1mg if 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](#)

### 28 day cycle for 6 cycles

#### Cycle 1

Drug	Dose	Days	Administration
Chlorambucil	6mg/m <sup>2</sup> (max 10mg)	1, 2, 3, 4, 5, 6, 7	Oral
Doxorubicin	50mg/m <sup>2</sup>	8	Intravenous bolus over 10minutes
Etoposide	75mg/m <sup>2</sup>	1, 2, 3, 4, 5	Oral
Prednisolone	50mg	1, 2, 3, 4, 5, 6, 7	Oral
Procarbazine	90mg/m <sup>2</sup> (max 200mg)	1, 2, 3, 4, 5, 6, 7	Oral
Vinblastine	6mg/m <sup>2</sup> (max 10mg)	8	Intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes
Vincristine	1.4mg/m <sup>2</sup> (max 2mg)	1	Intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

#### Cycle 2, 3, 4, 5, 6

The dose of etoposide is increased to 100mg/m<sup>2</sup> for five days with second or subsequent cycles if the oral mucositis is no worse than NCI-CTC grade 1 after the first exposure at 75mg/m<sup>2</sup>

Drug	Dose	Days	Administration
Chlorambucil	6mg/m <sup>2</sup> (max 10mg)	1, 2, 3, 4, 5, 6, 7	Oral
Doxorubicin	50mg/m <sup>2</sup>	8	Intravenous bolus over 10minutes
Etoposide	100mg/m <sup>2</sup>	1, 2, 3, 4, 5	Oral
Prednisolone	50mg	1, 2, 3, 4, 5, 6, 7	Oral
Procarbazine	90mg/m <sup>2</sup> (max 200mg)	1, 2, 3, 4, 5, 6, 7	Oral
Vinblastine	6mg/m <sup>2</sup> (max 10mg)	8	Intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes
Vincristine	1.4mg/m <sup>2</sup> (max 2mg)	1	Intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

## [Dose Information](#)

- Chlorambucil is available as 2mg tablets and will be rounded to the nearest 2mg (up if halfway)
- Chlorambucil tablets should be stored in a refrigerator

- Doxorubicin will be dose banded according to the national dose bands (2mg/ml)
- The maximum lifetime cumulative dose of doxorubicin is 450mg/m<sup>2</sup>. However prior radiotherapy to mediastinal/pericardial area should receive a lifetime cumulative doxorubicin dose of no more than 400mg/m<sup>2</sup>
- Etoposide is available as 50mg capsules. To facilitate alternate day dosing in ARIA the dose will be rounded to the nearest 25mg (up if halfway)
  - if the calculated daily dose is 125mg please dispense 150mg alternating with 100mg once a day
  - if the calculated daily dose is 175mg please dispense 200mg alternating with 150mg once a day
  - if the calculated dose is 225mg please dispense 250mg alternating with 200mg once a day
- Vinblastine dose will be dose banded according to the national dose bands (1mg/ml)
- The maximum dose of vinblastine is 10mg
- Vincristine will be dose banded according to the national dose bands (1mg/ml)
- The maximum dose of vincristine is 2mg
- Prednisolone is available as 5mg and 25mg tablets
- Procarbazine is available as 50mg capsules. The daily dose will be capped at 200mg. To facilitate alternate day dosing in ARIA the dose will be rounded to the nearest 25mg (up if halfway).
  - If the calculated daily dose is 125mg please dispense 150mg alternating with 100mg once a day
  - If the calculated daily dose is 175mg please dispense 200mg alternating with 150mg once a day

### Administration Information

#### *Extravasation*

- Doxorubicin – vesicant
- Vinblastine – vesicant
- Vincristine - vesicant

#### *Other*

- Chlorambucil may be taken at night to avoid daytime nausea
- Prednisolone should be taken in the mornings with or after food
- Procarbazine has weak MAOI activity. Alcohol and foods rich in tyramine (including some wines and cheeses) should be avoided. Do not use with other MAOIs.

### Additional Therapy

- Antiemetics

15-30 minutes prior to chemotherapy on day 1

- metoclopramide 10mg oral or intravenous

15-30 minutes prior to chemotherapy on day 8

- metoclopramide 10mg oral or intravenous
- ondansetron 8mg oral or intravenous

As take home medication day 1 only

- metoclopramide 10mg oral three times a day when required
- Allopurinol 300mg once a day oral for 7 days 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 H<sub>2</sub> antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

### Additional Information

- The National Patient Safety Agency report NPSA/2008/RRR04 must be followed in relation to intravenous administration of vinca alkaloids.
- 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.

### Coding

- Procurement – X70.3
- Delivery – X72.1 Day 1 + X72.4 Day 8

### References

1. ChIVPP therapy for Hodgkin's Disease: experience of 960 patients. The International ChIVPP Treatment Group. Ann. Oncol. 1995;6(2):167-172
2. Radford JA, Rohatiner ZS, Ryder JA et al. ChIVPP/EVA Hybrid Versus the Weekly VAPEC-B Regimen for Previously Untreated Hodgkin's Disease. J Clin Oncol 2002; 20 (13): 2988-2994.

## REGIMEN SUMMARY

### ChIVPP-EVA-Chlorambucil-Doxorubicin-Etoposide-Prednisolone- Procarbazine-Vinblastine-Vincristine

#### Cycle 1 Day One

1. **Warning – Check blood transfusion status**  
Administration Instructions  
Patients with HODGKIN'S lymphoma carry a lifelong risk of transfusion associated graft versus host disease. Where blood products are required these patients must receive ONLY IRRADIATED BLOOD PRODUCTS for life. Ensure transfusion departments are notified and the patient has been issued with an alert card to carry with them at all times.
2. **Warning – Do not cap doses**  
Administration Instructions  
ARIA automatically caps doses at  $2.4\text{m}^2$ . This is not recommended for this regimen. Please ensure that doses are not capped.
3. Metoclopramide 10mg oral or intravenous
4. Vincristine  $1.4\text{mg}/\text{m}^2$  (maximum 2mg) intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

#### Take Home Medicines

5. Chlorambucil  $6\text{mg}/\text{m}^2$  (max 10mg) once a day oral for 7 days  
Administration Instructions  
Oral chemotherapy.
6. Etoposide  $75\text{mg}/\text{m}^2$  once a day oral for 5 days  
Administration Instructions  
Oral chemotherapy.  
Etoposide is available as 50mg capsules. To facilitate alternate day dosing in ARIA the dose will be rounded to the nearest 25mg (up if halfway)
  - if the calculated daily dose is 125mg please dispense 150mg alternating with 100mg once a day
  - if the calculated daily dose is 175mg please dispense 200mg alternating with 150mg once a day
  - if the calculated dose is 225mg please dispense 250mg alternating with 200mg once a day
7. Prednisolone 50mg once a day oral for 7 days
8. Procarbazine  $90\text{mg}/\text{m}^2$  (max 200mg) once a day oral for 7 days  
Administration Instructions  
Oral chemotherapy  
Procarbazine is available as 50mg capsules. The daily dose will be capped at 200mg. To facilitate alternate day dosing in ARIA the dose will be rounded to the nearest 25mg (up if halfway).
  - If the calculated daily dose is 125mg please dispense 150mg alternating with 100mg once a day
  - If the calculated daily dose is 175mg please dispense 200mg alternating with 150mg once a day
9. Allopurinol 300mg once a day oral for 7 days
10. Metoclopramide 10mg three times a day oral when required  
Administration Instructions  
Please supply 28 tablets or an original pack

#### Cycle 1 Day Eight

11. Metoclopramide 10mg oral or intravenous



12. Ondansetron 8mg oral or intravenous
13. Doxorubicin 50mg/m<sup>2</sup> intravenous bolus over 10 minutes
14. Vinblastine 6mg/m<sup>2</sup> (maximum 10mg) intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

### Cycle 2, 3, 4, 5, 6 Day One

15. Warning – Do not cap doses  
Administration Instructions  
ARIA automatically caps doses at 2.4m<sup>2</sup>. This is not recommended for this regimen. Please ensure that doses are not capped.
16. Metoclopramide 10mg oral or intravenous
17. Vincristine 1.4mg/m<sup>2</sup> (maximum 2mg) intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

### Take Home Medicines

18. Chlorambucil 6mg/m<sup>2</sup> (max 10mg) once a day oral for 7 days  
Administration Instructions  
Oral chemotherapy.
19. Etoposide 100mg/m<sup>2</sup> once a day oral for 5 days  
Administration Instructions  
Oral chemotherapy.  
Etoposide is available as 50mg capsules. To facilitate alternate day dosing in ARIA the dose will be rounded to the nearest 25mg (up if halfway)
  - if the calculated daily dose is 125mg please dispense 150mg alternating with 100mg once a day
  - if the calculated daily dose is 175mg please dispense 200mg alternating with 150mg once a day
  - if the calculated dose is 225mg please dispense 250mg alternating with 200mg once a day
20. Prednisolone 50mg once a day oral for 7 days
21. Procarbazine 90mg/m<sup>2</sup> (max 200mg) once a day oral for 7 days  
Administration Instructions  
Oral chemotherapy  
Procarbazine is available as 50mg capsules. The daily dose will be capped at 200mg. To facilitate alternate day dosing in ARIA the dose will be rounded to the nearest 25mg (up if halfway).
  - If the calculated daily dose is 125mg please dispense 150mg alternating with 100mg once a day
  - If the calculated daily dose is 175mg please dispense 200mg alternating with 150mg once a day
22. Metoclopramide 10mg three times a day oral when required  
Administration Instructions  
Please supply 28 tablets or an original pack

### Cycle 2, 3, 4, 5, 6 Day Eight

23. Metoclopramide 10mg oral or intravenous
24. Ondansetron 8mg oral or intravenous
25. Doxorubicin 50mg/m<sup>2</sup> intravenous bolus over 10 minutes
26. Vinblastine 6mg/m<sup>2</sup> (maximum 10mg) intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

## DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	June 2018	None	Dr Debbie Wright Pharmacist	Dr Rob Lown 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 that occur as a result of following these guidelines. These protocols should be used in conjunction with other references such as the Summary of Product Characteristics and relevant published papers.