Chemotherapy Protocol

LYMPHOMA

CYCLOPHOSPHAMIDE-PREDNISOLONE-VINCRISTINE

(CVP)

Regimen

- Lymphoma – CVP-Cyclophosphamide-Prednisolone-Vincristine

Indication

- Non Hodgkin's Lymphoma

Toxicity

Drug	Adverse Effect
Cyclophosphamide	Dysuria, haemorrhagic cystitis (rare), taste disturbances
Prednisolone	Weight gain, GI disturbances, hyperglycaemia, CNS disturbances, cushingoid changes, glucose intolerance
Vincristine	Peripheral neuropathy, constipation, jaw pain

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

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

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 alone.

Neutrophils (x10^9/L)	**Dose Modifications (cyclophosphamide only)**
1 or greater	100%
0.5 – 0.9	1st Occurrence If no growth factor prophylaxis has been previously given then administer 100% of the doses with prophylactic growth factors An alternative approach, where the individual has a poor performance status or the intent in not curative is to delay until the neutrophils are 1x10^9/L and give 75% of the original dose as well as prophylactic growth factors 2nd Occurrence Delay until neutrophils are 1x10^9/L or above and then give 50% of the original dose as well as growth factors
Less than 0.5 or febrile neutropenia	1st Occurrence Delay until the neutrophils are 1x10^9/L or above and then give 75% of the original dose as well as prophylactic growth factors 2nd Occurrence Delay until neutrophils are 1x10^9/L or above and then give 50% of the original dose as well as growth factors
Platelets (x10^9/L)	**Dose Modifications (cyclophosphamide only)**
75 or above	100%
50 – 74	1st Occurrence Give 75% dose of the original dose 2nd Occurrence Give 50% dose of the original dose
Less than 50 or signs of active haemorrhage	1st Occurence Delay until the platelets are 75 or above then give 75% of the original dose 2nd Occurrence Delay until the platelets are 75 or above then give 50% of the original dose

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)
Cyclophosphamide	Evidence suggests dose modification not necessary.			
Vincristine	*30-51	or	60-180	50%
	more than 51	and	normal	50%
	more than 51	and	more than180	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 than10	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.

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 – 8 cycles (6 cycles will be set in ARIA)

Drug	Dose	Days	Administration
Cyclophosphamide	750mg/m^2	1	Intravenous bolus over 10 minutes
Vincristine	1.4mg/m^2 (max 2mg)	1	Intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes
Prednisolone	100mg	1, 2, 3, 4, 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
- Vincristine dose will be rounded to the nearest 0.1mg (up if halfway)
- The maximum dose of vincristine is 2mg

Administration Information

Extravasation

- Cyclophosphamide – neutral
- Vincristine - vesicant

Other

- Prednisolone should be taken in the morning with or after food

Additional Therapy

- Antiemetics

  15-30 minutes prior to chemotherapy

  - ondansetron 8mg oral or intravenous

  As 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 report NPSA/2008/RRR04 must be followed in relation to intravenous administration of vinca alkaloids.

Coding (OPCS 4.6)

- Procurement – X70.1

- Delivery – X72.3

References

1.Marcus R, Imrie K, Belch A et al. Chemotherapy plus rituximab compared with CVP as first line treatment for advanced follicular lymphoma. Blood 2005: 105 (4); 1417-1423.

REGIMEN SUMMARY

CVP-Cyclophosphamide-Prednisolone-Vincristine

Cycle 1

1. Ondansetron 8mg oral or intravenous injection
2. Prednisolone 100mg oral
3. Vincristine 1.4mg/m^2 (max 2mg) intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes
4. Cyclophosphamide 750mg/m^2 intravenous bolus over 10 minutes

Take Home Medicines

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

Cycles 2, 3, 4, 5 and 6

1. Ondansetron 8mg oral or intravenous injection
2. Prednisolone 100mg oral
3. Vincristine 1.4mg/m^2 (max 2mg) intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes
4. Cyclophosphamide 750mg/m^2 intravenous bolus over 10 minutes

Take Home Medicines

5. Prednisolone 100mg once a day for 4 days (starting on day 2) oral
6. Metoclopramide 10mg three times a day when required oral
7. 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 Bolus 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	Page 4. "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.