Chemotherapy Protocol

LYMPHOMA

CYCLOPHOSPHAMIDE–FLUDARABINE INTRAVENOUS

(FC IV 3 day)

Regimen

- Lymphoma – FC IV (3 day)- Cyclophosphamide-Fludarabine IV (3 day)

Indication

- Non-Hodgkin Lymphoma

Toxicity

Drug	Adverse Effect
Cyclophosphamide	Dysuria, haemorrhagic cystitis (rare), taste disturbances
Fludarabine	Transfusion related GVHD, neurotoxicity, opportunistic infections, GI disturbances

Patients treated with fludarabine 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 the decision to treat is made and the patient must be issued with an alert card to carry with them at all times.

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
- Direct Coombs test prior to starting 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. **Irradiated blood products must be used (fludarabine).**

Dose modifications based on haematological parameters apply to cyclophosphamide and fludarabine

Neutrophils ($x10^9$/L)	**Dose Modifications**
greater than or equal to 1	100%
less than 1	1st Occurrence. Delay until recovery and then give 75% of the original dose 2nd Occurrence Delay until recovery and then give 50% of the original dose.
Platelets ($x10^9$/L)	**Dose Modifications**
greater than or equal to 75	100%
Less than 75	1st Occurrence. Delay until recovery and then give 75% of the original dose 2nd Occurrence Delay until recovery and 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	Recommendation
Cyclophosphamide	Evidence suggests no dose modification necessary
Fludarabine	No dose adjustment required

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Cyclophosphamide	greater than 20	100%
	10-20	75%
	less than 10	50%
Fludarabine	greater than 70	100%
	30-70	50%
	less than 30	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.

Regimen

28 day cycle for up to 6 cycles

Drug	Dose	Days	Administration
Cyclophosphamide	250mg/m^2	1,2,3	Intravenous bolus over 10 minutes
Fludarabine	25mg/m^2	1,2,3	Intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes

Dose Information

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

Administration Information

- Cyclophosphamide - neutral
- Fludarabine - neutral

Additional Therapy

- Antiemetics

15-30 minutes prior to chemotherapy

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

As take home medication

- metoclopramide 10mg oral three times a day when required
- ondansetron 8mg oral each evening for 3 days then twice a day for 2 days

- Allopurinol 300mg once a day oral for the first cycle only
- Anti-infective prophylaxis as follows:

  - aciclovir 400mg twice a day oral
  - co-trimoxazole 960mg once a day oral on Monday, Wednesday and Friday only continued for 6 months after the completion of treatment or in accordance with CD4 count.

  Please note that patients treated with fludarabine are at higher risk of fungal and atypical infections. A high level of suspicion must be maintained coupled with a low threshold for prompt and appropriate treatment.

- Mouthwashes according to local or national policy on the treatment of mucositis
- 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.

Coding (OPCS 4.6)

- Procurement – X70.3
- Delivery – X72.3, X72.4

References
1. Eucker J,Schille C,Schmid P, et al. The combination of fludarabine and cyclophosphamide results in a high remission rate with moderate toxicity in low grade non Hodgkin's lymphomas. AntiCancer Drugs 2002;13:907–13.
2. MRC CLL4 Trial. A randomised comparison of chlorambucil, fludarabine and fludarabine plus cyclophosphamide. 2001.

REGIMEN SUMMARY

FC IV (3 day)-Cyclophosphamide-Fludarabine IV (3 day)

Cycle 1 Day 1

1. Warning – Check blood transfusion status
   Administration Instructions
   Patients treated with fludarabine 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. Metoclopramide 10mg oral or intravenous

3. Ondansetron 8mg oral or intravenous

4. Cyclophosphamide 250mg/m^2 intravenous bolus over 10 minutes

5. Fludarabine 25mg/m^2 intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes

Take home medicines

6. Allopurinol 300mg once a day for oral 28 days

7. Aciclovir 400mg twice a day oral for 28 days

8. Co-trimoxazole 960mg once a day oral on Mondays, Wednesdays and Fridays for 28 days

9. Metoclopramide 10mg three times a day oral when required

10. Ondansetron 8mg every evening oral for 3 days starting on day one of treatment, then 8mg twice a day oral for 2 days.

Cycle 1 Day 2 and 3

1. Metoclopramide 10mg oral or intravenous

2. Ondansetron 8mg oral or intravenous

3. Cyclophosphamide 250mg/m^2 intravenous bolus over 10 minutes

4. Fludarabine 25mg/m^2 intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes

Cycles 2, 3, 4, 5, and 6 Day 1

1. Metoclopramide 10mg oral or intravenous
2. Ondansetron 8mg oral or intravenous
3. Cyclophosphamide 250mg/m^2 intravenous bolus over 10 minutes
4. Fludarabine 25mg/m^2 intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes

Take home medicines

5. Aciclovir 400mg twice a day oral for 28 days
6. Co-trimoxazole 960mg once a day oral on Mondays, Wednesdays and Fridays for 28 days
7. Metoclopramide 10mg three times a day oral when required
8. Ondansetron 8mg every evening oral for 3 days starting on day one of treatment, then 8mg twice a day oral for 2 days.

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

1. Metoclopramide 10mg oral or intravenous
2. Ondansetron 8mg oral or intravenous
3. Cyclophosphamide 250mg/m^2 intravenous bolus over 10 minutes
4. Fludarabine 25mg/m^2 intravenous infusion in 100ml sodium chloride 0.9% over 30 minutes

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	Jan 2015	Header changed Toxicities removed “a diagnosis” replaced with “the decision to treat” in TA-GVHD warning Hepatic and renal impairment tables updated Metoclopramide dose changed to 10mg Bolus removed from intravenous bolus throughout text Mucositis recommendation changed “Warning-Check blood transfusion status” added to cycle 1 Disclaimer added	Donna Kimber Pharmacy Technician	Rebecca Wills Pharmacist
1	May 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.