

Chemotherapy Protocol

LYMPHOMA

CYCLOPHOSPHAMIDE-FLUDARABINE ORAL 5 DAY

(FC PO 5 day)

Regimen

- Lymphoma – FC PO (5 day)-Cyclophosphamide-Fludarabine PO (5 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	1 st Occurrence. Delay until recovery and then give 75% of the original dose 2 nd 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	1 st Occurrence. Delay until recovery and then give 75% of the original dose 2 nd 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.

Severe Nausea and Vomiting

Consider changing to an intravenous version of this regimen if severe nausea and vomiting becomes a problem.

Regimen

28 day cycle for up to 6 cycles

Drug	Dose	Days	Administration
Cyclophosphamide	150mg/m ²	1,2,3,4,5	Oral
Fludarabine	24mg/m ²	1,2,3,4,5	Oral

Dose Information

- Cyclophosphamide is available as 50mg tablets and will be rounded to the nearest 50mg (up if halfway).
- Fludarabine is available as 10mg tablets and will be rounded to the nearest 10mg (up if halfway).

Administration Information

- Cyclophosphamide should be taken with breakfast, swallowed whole with a full glass of water
- Fludarabine should be taken with lunch, swallowed whole with a full glass of water

Additional Therapy

- Antiemetics

As take home medication

- Ondansetron 8mg oral twice a day for 7 days
 - Metoclopramide 10mg oral three times a day when required
- Allopurinol 300mg once a day oral for the first cycle only
 - Anti-infective prophylaxis as follows:
 - aciclovir 400mg twice a day
 - 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 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.

Coding (OPCS 4.6)

- Procurement – X70.3
- Delivery – X73.1

References

- 1.Fabbri A, Lenoci M, Gozzetti A et al. Low-dose oral fludarabine plus cyclophosphamide as first-line treatment in elderly patients with indolent non-Hodgkin lymphoma.; Br J Haem 2007; 139; 90 – 93.
- 2.MRC CLL4 Trial. A randomised comparison of chlorambucil, fludarabine and fludarabine plus cyclophosphamide. 2001.

REGIMEN SUMMARY

FC PO (5 day)-Cyclophosphamide-Fludarabine PO 5 day

Cycle 1

Take Home Medicines

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. Cyclophosphamide 150mg/m² once a day oral for 5 days
3. Fludarabine 24mg/m² once a day oral for 5 days
4. Allopurinol 300mg once a day oral for 28 days
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 twice a day for 7 days oral starting prior to the first dose of oral chemotherapy

Cycles 2, 3, 4, 5, and 6

Take Home Medicines

1. Cyclophosphamide 150mg/m² once a day for 5 days oral
2. Fludarabine 24mg/m² once a day for 5 days oral
3. Aciclovir 400mg twice a day oral for 28 days
4. Co-trimoxazole 960mg once a day oral on Mondays, Wednesdays and Fridays for 28 days
5. Metoclopramide 10mg three times a day oral when required
6. Ondansetron 8mg twice a day for 7 days oral starting prior to the first dose of oral chemotherapy

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 Ondansetron TTO clarified 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.