

FLUDARABINE (based on the MRC CLL4 trial)

INDICATION: CLL, follicle centre cell lymphoma, lymphoplasmacytic lymphoma

Prior to a course of treatment

- If creatinine is raised check creatinine clearance – *see dose modification*
- Check FBC. Patient should have adequate bone marrow reserve, i.e neutrophils > 1.0, platelets >75 unless cytopaenia is due to disease, e.g marrow infiltration, splenomegaly
- If appropriate discuss possibility of pregnancy with female patients and need for contraception with both male and female patients. Discuss risk of infertility - offer semen cryopreservation to males
- Inform transfusion lab that irradiated blood products will be required
- Written consent for course

Prior to each cycle

- Medical review of fitness for chemotherapy – exclude active infection, major changes in organ function
- Check FBC - neutrophils should be >1.0 and platelets >75 (*see dose modification*)
- Check U&Es, creat – if previous fludarabine dose reduction consider gradual escalation according to renal function and haematological toxicity in earlier cycles

Oral version

Fludarabine *	40mg/m ²	PO	od for 5 days
* 10mg tablets			

Nausea and diarrhoea are common with oral fludarabine. The IV form may be better tolerated.

Intravenous version

Fludarabine	25mg/m ² in 100ml N saline	IV over 30mins	od for 5 days
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Repeat cycle every 28 days for up to 8 cycles

Prophylaxis for acute emesis

Not required

Prophylaxis for delayed emesis

Metoclopramide for 3-4 days (*do not use dexamethasone*)

Other medications

Allopurinol 300mg od for 7 days with cycle 1

Cotrimoxazole 480mg od until 6 months after completion

Dose modifications for haematological toxicity (unless due to disease)

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| • Day 28 neuts <1.0 or plats <75 | Delay treatment for up to 2 weeks & reduce dose of fludarabine by 25% for subsequent cycles if counts recover |
| • Neuts 0.5-1.0 or plats 50-75 despite 2 weeks delay | Proceed with chemotherapy at 50-75% dose |
| • Day 28 neuts 0.5-1.0 or plats 50-75 despite 25% dose reduction | Reduce to 50% original doses of fludarabine |
| • Neuts <0.5 or plats <50 when next course due | Delay treatment until these levels reached with dose modifications as above if necessary |

Growth factor support with GCSF may be appropriate in some cases - *discuss with consultant*

Dose modification for renal dysfunction

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|------------------------------------|----------------------|
| • Creatinine clearance 30-60ml/min | 50% dose fludarabine |
| • Creatinine clearance <10ml/min | Stop fludarabine |

Fludarabine Toxicities

Neutropenic sepsis	Nausea (none-mild)
Thrombocytopenia	Amenorrhoea & infertility (offer semen cryopreservation)
Auto-immune haemolysis	Opportunistic infection
Diarrhoea	Encephalopathy – coma, cortical blindness (rarely)

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