# FMD

Second-line treatment for indolent forms of Non Hodgkins Lymphoma

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| Drugs / Dosage: | **Fludarabine** | 40mg/m$^2$ | PO once daily | D1 to D3 |
| | **Mitoxantrone** | 10mg/m$^2$ | IV | D1 |
| | **Dexamethasone** | 20mg | IV or PO once daily | D1 to D5 |

If the oral route is contra-indicated, substitute oral fludarabine with:

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| **Fludarabine** | 25mg/m$^2$ | IV | D1 – D3 |

Reduce doses of fludarabine and mitoxantrone by 20% if age > 65 years, prior extensive radiotherapy or poor haematological tolerance to prior chemotherapy

Administration: Mitoxantrone diluted in 0.9% Sodium Chloride and administered via a fast-running infusion of 0.9% Sodium Chloride.
Fludarabine available as 10mg tablets, to be swallowed whole with water, or intravenously by slow bolus injection

**Other drugs:** Allopurinol 300mg po daily, ideally starting 24 hours before chemotherapy - review after 4 weeks
PCP prophylaxis - prescribe according to unit practice/protocol (generally until 6 months after completion of treatment, or according to $CD_4$ counts)
Fluconazole for antifungal prophylaxis
Use of proton pump inhibitor or $H_2$ receptor antagonist (e.g. ranitidine) is recommended whilst treating with steroids.
Consider aciclovir prophylaxis if history of VZV or HSV reactivation

Frequency: 4 weekly cycle for 6 – 8 cycles

Main Toxicities: myelotoxicity; opportunistic infections; alopecia; mucositis; acute tumour lysis syndrome - pre-treat with allopurinol & advise high fluid intake; if bulky disease or rapid response expected, pre-treat in hospital with iv fluids; autoimmune haemolytic anaemia (fludarabine – see Comments); cardiomyopathy (see Comments); ovarian failure; infertility

Anti – emetics: Moderately emetogenic (but anti-emetic doses of dexamethasone are not required due to high dose dexamethasone)

Extravasation: Non-vesicants

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| Regular Investigations: | FBC | D1 |
| | LFTs & U&Es | D1 |
| | LDH | D1 |
| | MUGA/echo | see Comments |
| | Blood glucose | see Comments |
| | Blood pressure | see Comments |
| | DAT } | baseline, and repeat if disproportionate anaemia or |
| | Reticulocytes } | any history of autoimmune haemolytic anaemia (AHA) |
| | Bilirubin } | (see Comments) |

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| Prepared by Oncology Pharmacist: S Taylor | Checked by Network Pharmacist: pp Carolyn Tucker |

Comments: Maximum cumulative dose of mitoxantrone = 160mg/$m^2$
A baseline MUGA scan/echo should be performed where the patient is considered at risk of having impaired cardiac function e.g. significant cardiac history, hypertension, obese, smoker, elderly, previous exposure to anthracyclines, previous thoracic radiotherapy. MUGA/echo should be repeated if there is suspicion of cardiac toxicity at any point during treatment, or if cumulative dose of mitoxantrone and any previous anthracyclines approaches maximum.

All patients must receive irradiated blood products for all future transfusions - inform patient and blood bank.

Patients undergoing treatment with fludarabine should be closely monitored for signs of AHA. Fludarabine should be used with caution if DAT positive in the absence of haemolysis.

In patients presenting with both leukaemia and haemolysis, the patient should usually first be treated to control haemolysis before commencing fludarabine. If the haemolysis subsequently re-occurs / worsens, then discontinuation of fludarabine is recommended.

Blood glucose and blood pressure monitoring to be tailored according to individual patient needs.

**Dose Modifications**

Haematological Toxicity: If neutrophils < 1.5 x $10^9$/L or platelets < 100 x $10^9$/L, delay treatment for 1 week. If FBC not recovered after 2 weeks, give a 20% dose reduction for future cycles (see below), or consider alternative treatment. If in doubt, discuss with Consultant

Fludarabine and mitozantrone doses to be reduced by 20% for all subsequent courses if any of the following occur at any point during a cycle:
platelet count < 20 x $10^9$/L or mucosal bleeding
granulocyte count < 0.1 x $10^9$/L
episode of sepsis
delayed recovery of FBC > 35 days

Renal Impairment: Use Cockcroft & Gault formula for predicting creatinine clearance.

| CrCl (ml/min) | Fludarabine Dose |
|---|---|
| > 70 | Give 100% dose |
| 30 – 70 | Give 50% dose |
| < 30 | Omit |

Hepatic Impairment: Mitozantrone is not recommended with severe hepatic insufficiency or if bilirubin > 60µmol/l. If in doubt, discuss with Consultant.

Patient Information: CancerBACUP Leaflets for Fludarabine and Mitozantrone

Reference: McLaughlin, P et al (1996); JCO; 14: 1262 – 1268

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