FLUDARABINE

Second-line therapy for B-cell CLL for patients who have either failed or are intolerant of first-line chemotherapy – NICE approved 2001
Second-line treatment for Waldenstrom's macroglobulinaemia

Drug/Dosage: **Fludarabine** 40mg/m^2 PO Daily on Days 1, 2, 3, 4 and 5

or, if the oral route is contra-indicated,
Fludarabine 25mg/m^2 IV Daily on Days 1, 2, 3, 4 and 5

Administration: 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)
Consider aciclovir prophylaxis if history of VZV or HSV reactivation

Frequency: Cycle repeat 4 weekly
Assess for response after 2 cycles: If no response, discontinue
Continue for maximum of 6 cycles in responders

Main Toxicities: myelotoxicity; opportunistic infections;
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);
ovarian failure; infertility

Anti-emetics: Mildly emetogenic

Extravasation: Non- vesicant

Regular Investigations:

FBC		Day 1
U&Es		Day 1
LFTs		Day 1
LDH		Day 1
DAT	}	baseline, and repeat if disproportionate anaemia or
Reticulocytes	}	any history of autoimmune haemolytic anaemia (AHA)
Bilirubin	}	(see Comments)

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

Reason for Update: Prepared for Network use	Approved by Chair of Network TSSG: Dr A Laurie
Version: 1	Date: 23.2.06
Supersedes: All previous versions	Review date: February 2008
Prepared by Oncology Pharmacist: S Taylor	Checked by Network Pharmacist: Jacky Turner

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.

Dose Modifications

Haematological Toxicity:

Cycle 1: Give 50% dose if heavy prior treatment with alkylating agents or neutrophils < 1.0 x 10^9/l or platelets < 50 x10^9/l

Subsequent cycles: Defer for one week if neutrophils < 1.0 x 10^9/l or platelets < 50 x 10^9/l. Repeat FBC and proceed if counts have recovered.

If low counts are thought to be due to marrow infiltration, discuss with Consultant.

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

Creatinine clearance (ml/min)	**Fludarabine Dose**
> 70	Give 100% dose
30 – 70	Give 50% dose
< 30	Omit

Patient Information: CancerBACUP leaflet for Fludarabine

Reference: Keating et al; Blood 1989, 74:19 – 25