Imatinib for CML and Ph+ ALL		
Indication	1st line treatment of Philadelphia positive (Ph+) CML in the chronic, accelerated or blast crisis phase (where bone marrow transplantation as is not considered as 1st line treatment). Imatinib is recommended as an option for patients who present in the chronic phase and then progress to the accelerated phase or blast crisis if they have not received imatinib previously .N.B. High dose imatinib (that is 600mg in the chronic phase or 800mg in the accelerated and blast-crisis phases) is **not** recommended for treating Ph+ CML in patients who are imatinib resistant. 1st line treatment of Ph+ ALL in combination with chemotherapy (usually Induction Phase prior to allograft)	
Antineoplastic agent	Imatinib	CML Chronic phase: 400mg orally once daily Accelerated or blast crisis 600mg orally daily with a meal and a large glass of water Ph+ ALL 600mg orally once daily For patients unable to swallow the tablets, disperse tablets in mineral water or apple juice
Drug Interactions (see SPC for full list http://emc.medicines.org.uk/)	Drugs that inhibit or induce cytochrome P450 isoenzyme CYP3A4 activity could affect imatinib concentrations. The following drugs increase plasma levels of imatinib: clarithromycin, erythromycin, itraconazole. The following drugs decrease plasma levels of imatinib: carbamazepine, dexamethasone, phenytoin. Drugs whose plasma levels may be increased by imatinib: ciclosporin, statins, warfarin. Imatinib may inhibit the metabolism of warfarin, consider using a low molecular weight or unfractionated heparin in patients requiring anticoagulation. Monitor liver function carefully if on concomitant hepatotoxic medications. Grapefruit juice should be avoided; increased imatinib plasma concentration. Aprepitant- potentially elevated plasma levels of imatinib. Levothyroxine- decreased effectiveness, worsening hypothyroidism.	
Length of treatment	CML Continuous until progression of disease or no longer tolerated Ph+ ALL In combination with chemotherapy in the induction, consolidation and maintenance phases of chemotherapy, duration may vary.	

Imatinib for CML and Ph+ ALL		
Dose modifications		Chronic Phase CML (starting dose 400mg):
	Neutrophils < 1.0 x 10^9/L and/or platelets < 50 x 10^9/L	Stop imatinib until neutrophils ≥ 1.5 x 10^9/L and platelets ≥ 75 x 10^9/L. Resume treatment at current dose level. In the event of a recurrence stop imatinib until counts recover as above and resume at a dose of 300mg
		Accelerated phase or blast crisis CML and Ph+ ALL (starting dose 600mg):
	Neutrophils < 0.5 x 10^9/L and/or platelets < 10 x 10^9/L	Check whether cytopenia is related to leukaemia (BM aspirate or biopsy). If unrelated to leukaemia reduce dose to 400mg. If cytopenia persists for 2 weeks reduce further to 300mg. If cytopenia persists at 4 weeks then stop imatinib until neutrophils ≥ 1.0 x 10^9/L and platelets ≥ 20 x 10^9/L. Resume treatment at a dose of 300mg
	Impaired liver function	For any degree of hepatic impairment start at 400mg daily and adjust for toxicities. If during treatment bilirubin > 3 x ULN or AST/ALT > 5 x ULN hold until bilirubin < 1.5 ULN and AST/ALT < 2.5 x ULN then resume treatment at: Chronic phase CML – 300mg daily Accelerated phase or blast crisis CML – 400mg daily ALL – 400mg daily
	Impaired renal function	Patients with renal dysfunction or on dialysis should be given the minimum recommended dose of 400mg daily with caution. Dose can be reduced if not tolerated. If tolerated the dose can be increased for lack of efficacy.
	Non-haematological toxicity	If a severe non-haematological adverse reaction develops, treatment must be withheld and may be resumed if appropriate, depending on the initial severity of the event.
Mandatory tests	FBC, LFT, U&E	CML: Weekly for the first 4 weeks then every 2-3 weeks until complete haematological response then every 4-12 weeks. ALL: As indicated by chemotherapy regimen.
	Hepatitis B serology should be tested before starting treatment.	
Mandatory supportive drugs	Allopurinol if WCC >100 x 10^9/L (or if indicated with chemotherapy protocol)	

Mandatory information	Patients should be supplied with a patient information leaflet, Cancerbackup information sheet and a copy of their treatment plan

Ratifying consultant (Chair of NOG): Maadh Aldouri
Pharmacists: J Sawyer & C Waters
Version 2
Review April 2018