IMATINIB MESYLATE

INDICATIONS: Philadelphia positive CML, hypereosinophilic syndrome, Philadelphia positive ALL

Prior to a course of treatment

- FBC, U&Es, creat, LFTs, CXR
- If appropriate discuss possibility of pregnancy with female patients and need for contraception with both male and female patients.
- There is little information on the effect on fertility. Discuss risk of infertility - offer semen cryopreservation to males
- Consent for course

Prior to each prescription

- Monitor FBC, U&Es, creat, LFTs weekly for the first month. In the absence of significant myelosuppression or toxicity the frequency of testing can be reduced
- Medical review of fitness for chemotherapy – exclude active infection, major changes in organ function

Chronic myeloid leukaemia - chronic phase		
Imatinib mesylate	400mg PO od	continuously until disease progression or intolerance
Chronic myeloid leukaemia – accelerated and blast phase		
Imatinib mesylate	600mg PO od *	continuously until disease progression or intolerance
	*increase to 400mg bd may be considered	
Hypereosinophilic syndrome		
Imatinib mesylate	100mg PO od	continuously until disease progression or intolerance
Ph +ve acute lymphoblastic leukaemia		
Imatinib mesylate	400mg PO od initially, increased to 600mg od according to tolerance	For up to 18 months as maintenance

Prophylaxis for acute & delayed emesis	Metoclopramide 10 – 20mg 6-8 hourly
Other medications	Consider allopurinol 300mg od especially for hyperleucocytosis and advanced phases

Dose modification for haematological toxicity (unless considered due to marrow infiltration)

Chronic phase	neuts > 1.0 and plats	100% dose
	neuts < 1.0 or plats < 50	Stop until neuts > 1.5 or plats > 75 then: 1st occurrence – resume at 400mg od 2nd occurrence – resume at 300mg od
Accelerated/blast phase	neuts >0.5 and plats > 10	100% dose
	neuts < 0.5 or plats < 10	• If not related to disease – reduce to 400mg od • If persists > 2 weeks – reduce to 300mg od • If persists > 4 weeks – stop until neuts > 1.0 or plats > 20, then resume at 300mg od
	Consider GCSF and platelet support for persistent or recurrent neutropenia and thrombocytopaenia, especially for advanced phase disease	

Dose modification for hepatic toxicity

Bilirubin < 3 x ULN and AST/ALT < 5 x ULN	100% dose
Bilirubin > 3 x ULN or AST/ALT > 5 x ULN	Stop until bilirubin < 1.5 and AST/ALT < 2.5 x ULN then: • resume at 300mg od for chronic phase • resume at 400mg od for accelerates/blast phase

Dose modification for renal failure

No initial dose reduction required – but note imatinib may cause renal toxicity and dose reduction may be indicated

Imatinib Toxicities

Anaemia, neutropaenia, thrombocytopaenia	Weight gain, oedema – including periorbital and serous effusions
Hepatotoxicity	Congestive cardiac failure
Rash, pruritus	Fatigue
Anorexia	Nausea, vomiting
Diarrhoea	Myalgia, bone pain, arthralgia

Drug Interactions: Imatinib is a potent inhibitor of cytochrome P450 and is also metabolized predominantly by cytochrome P450. Hence review concomitant medications. Major inducers e.g carbamazepine, dexamethasone, phenytoin, St John's Wort, rifampicin, may reduce levels. Inhibitors e.g cimetidine, erythromycin, itraconazole, verapamil, grapefruit juice, may increase levels. Imatinib may increase the anticoagulant effect of warfarin.

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