Bosutinib

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		
Bosutinib	500mg PO od	continuously until disease progression or intolerance
Chronic myeloid leukaemia – accelerated and blast phase		
Bosutinib	500mg PO od *	continuously until disease progression or intolerance
	*increase to 600mg may be considered	

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: Resume treatment with same dose if recovery within 2 weeks. If blood count remains low >2weeksupon recovery reduce dose by 100mg and resume treatment. If cytopenia recurs reduce dose by additional 100mg upon recovery and resume treatment
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

If liver transaminases greater than 5XULN occur hold dosing until recovery to <2.5XULN and resume at 400mg od,discontinue if recovery takes longer than 4 weeks.

Discontinue if transaminases>3XULN with bilirubin >x2ULN.

Dose modification for renal failure

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

Bosutinib Toxicities

Anaemia, neutropaenia, thrombocytopaenia	Abnormal LFT
	Neutropenic sepsis
Diarrhea (82%)	Edema
Rash, pruritus	Fatigue
Anorexia	Nausea, vomiting

Drug Interactions: Bosutinib 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. Bosutinib may increase the anticoagulant effect of warfarin.

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