Nilotinib

INDICATION:

- Newly diagnosed CML in chronic phase
- Chronic phase or accelerated phase CML with resistance or intolerance to prior therapy including imatinib

Prior to a course of treatment

- Note nilotinib is to be used in conjunction with network guidelines for management of CML
- Ensure imatinib has been discontinued at least 7 days before staring nilotinib
- Nilotinib should be used with caution in patients who have or who are at significant risk of developing prolongation of QTc, such as those:
  - with congenital long QT prolongation;
  - with uncontrolled or significant cardiac disease including recent myocardial infarction, congestive heart failure, unstable angina or clinically significant bradycardia;
  - taking anti-arrhythmic medicinal products or other substances that lead to QT prolongation.
- Avoid concomitant treatment with potent CYP3A4 inhibitors e.g. ketoconazole, itraconazole, voriconazole, ritonavir, moxifloxacin, clarithromycin and telithromycin
- Rifampicin and drugs that increase gastric pH e.g. proton pump inhibitors and H_2 antagonists may reduce the effectiveness of nilotinib
- Discuss the possible risk of teratogenicity and need for contraception with both male and female patients
- Written consent for course

Prior to each prescription

- Medical review of fitness for chemotherapy – exclude active infection, major changes in organ function
- For first 2 months: every 2 weeks before each prescription: FBC, U&Es, LFTs, serum lipase
- Subsequently – every 4 weeks before each prescription: FBC, U&Es, LFTs, serum lipase
- BCR-ABL transcript monitoring every 3 months

Nilotinib	300mg bd	PO (1st line treatment)
Nilotinib	400mg bd	PO (resistant disease or intolerance to prior therapy)

Continue treatment until disease progression or intolerance

Tablets should be taken 2 hours before food and patients should not eat until 1 hour after a dose

Prophylaxis for acute & delayed emesis	None
Other medications	None

Dose modifications for haematological toxicity

Neutrophils <0.5 and/or platelet counts <10	Treatment with nilotinib must be interrupted and blood count monitored. Treatment must be resumed within 2 weeks at prior dose if neuts>1.0 x 10^9/l and/or platelets>20 x 10^9/l. If blood counts remain low, a dose reduction to 400 mg once daily may be required.

Dose modifications for non-haematological toxicity

If clinically significant moderate or severe non-haematological toxicity develops, dosing should be interrupted, and may be resumed at 400 mg once daily once the toxicity has resolved. If clinically appropriate, re-escalation of the dose to the starting dose of 400 mg twice daily should be considered.

Elevated serum lipase: For Grade 3-4 serum lipase elevations, doses should be reduced to 400 mg once daily or interrupted. Serum lipase levels should be tested monthly or as clinically indicated

Elevated bilirubin and hepatic transaminases: For Grade 3-4 bilirubin and hepatic transaminase elevations, doses should be reduced to 400 mg once daily or interrupted. Bilirubin and hepatic transaminases levels should be tested monthly or as clinically indicated

Nilotinib toxicities

Neutropenia (14%)	Anaemia
Thrombocytopaenia (21%)	
Nausea (~1%)	Fatigue (~1.5%)
Rash (~3%)	Liver dysfunction (Hyperbilrubinemia 4.1% raised ALT2.1%; raised AST- 0.8%)
Headache (2%)	Diarrhoea
Hyperamylasemia (0.8%)	Hypertension
Cardiac: angina, arrhythmias, palpitations	Hyperlipasemia (6.5%) Hyperglycemia- 0.8%)

(% from ENACT Trial selected 1st Grade 3-4 AEs)

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