Nilotinib for second line therapy for Philadelphia Chromosome positive CML

Indication:

Chronic or accelerated phase chronic myeloid leukaemia (CML), failed or intolerant (grade 3 to 4 adverse events) to imatinib.

NICE TA 241

Regimen details:

Nilotinib 400 mg twice daily orally continuous

Administration:

Orally
Available as 200mg strength capsules.
Capsules should be taken twice daily approximately 12 hours apart.
Capsules should be swallowed whole with water.
Nilotinib should not be taken with food. No food should be consumed for 2 hours before the dose is taken and for at least one hour after the dose is taken.

For patients who are unable to swallow capsules, the content of each capsule may be dispersed in one teaspoon of apple sauce and should be taken immediately.

Premedication:

None required

Frequency:

Continuous (28 day cycles)

Extravasation:

Not applicable

Anti- emetics:

Minimal emetogenic potential (< 10%)

Supportive medication:

Allopurinol 100 - 300 mg od (dependent on renal function) for first 2 to 3 cycles

Regular investigations:

FBC D1 Initially every 2 weeks, less frequently as treatment stabilises.
LFTs D1
U&Es D1

Precautions for use:

Use 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 MI, CHF, unstable angina or clinically significant bradycardia
- taking anti-arrhythmic medicines
Close monitoring for an effect on the QTc interval is advisable, baseline ECG prior to initiating therapy. Hypokalaemia or hypomagnesaemia must be corrected prior to and during therapy.
Dose Modifications

Haematological Toxicity

Chronic phase CML (i.e. starting dose 400mg twice daily):

<table>
<thead>
<tr>
<th>Neutrophils</th>
<th>Platelets</th>
<th>Nilotinib</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1.0 x 10⁹/L &amp; ≥ 50 x 10⁹/L</td>
<td>100% dose</td>
<td></td>
</tr>
<tr>
<td>&lt; 1.0 x 10⁹/L or &lt; 50 x 10⁹/L</td>
<td>Stop treatment. If neutrophils ≥ 1.0 x 10⁹/L and/or platelets ≥ 50 x 10⁹/L within 2 weeks, resume treatment with 400mg bd.</td>
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</table>

If blood counts remain low, a dose reduction to 400mg od may be required.

Accelerated phase CML (i.e. starting dose 400mg twice daily):

<table>
<thead>
<tr>
<th>Neutrophils</th>
<th>Platelets</th>
<th>Nilotinib</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 0.5 x 10⁹/L &amp; ≥ 10 x 10⁹/L</td>
<td>100% dose</td>
<td></td>
</tr>
<tr>
<td>&lt; 0.5 x 10⁹/L or &lt; 10 x 10⁹/L</td>
<td>Stop treatment. If neutrophils ≥ 1.0 x 10⁹/L and/or platelets ≥ 20 x 10⁹/L within 2 weeks, resume treatment with 400mg bd.</td>
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</tbody>
</table>

If blood counts remain low, a dose reduction to 400mg od may be required.

Renal Impairment

No dose reduction necessary

Hepatic Impairment

Use with caution – may have increased exposure to nilotinib.

Toxicities:

Skin rash, nausea, fatigue, headache, constipation, diarrhoea, vomiting, muscle spasms, arthralgia, bone pain, peripheral oedema.

Elevation in serum lipase. Caution is therefore recommended in patients with a history of pancreatitis.

Drug interactions:

Nilotinib is a substrate and an inhibitor of CYP3A4. Therefore, there is potential for interaction with other concomitantly administered medicinal products that are metabolised primarily by or modulate the activity of CYP3A4.

The following drugs increase levels of nilotinib: clarithromycin, erythromycin, itraconazole, voriconazole. The following drugs decrease plasma levels of nilotinib: carbamazepine, phenytoin, rifampicin.

Use with caution in patients taking anti-arrhythmic agents e.g amiodarone, disopyramide, procainamide, quinidine, sotalol or other agents that may lead to QT prolongation e.g. clarithromycin, haloperidol, methadone, moxifloxacin.

Comments:

The bioavailability of nilotinib is increased by food. Nilotinib should not be taken with food and should be taken 2 hours after a meal. No food should be consumed for at least 1 hour after a dose is taken.
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Reason for Update: NICE TA241 Update haematological toxicity
SPC

References:
NICE TA241 Dasatinib, high-dose imatinib and nilotinib for the treatment of imatinib-resistant chronic myeloid leukaemia (CML) (part review of NICE technology appraisal guidance 70), and dasatinib and nilotinib for people with CML for whom treatment with imatinib has failed because of intolerance January 2012