

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Nilotinib for the first line treatment of chronic myeloid leukaemia

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of nilotinib within its licensed indication for the first line treatment of chronic myeloid leukaemia.

Background

Chronic myeloid (or myelogenous) leukaemia (CML) is characterised by production of an excessive number of white cell precursors by the bone marrow. CML is a progressive disease characterised by three identifiable phases: the chronic phase, the accelerated phase and the blast crisis (transformation) phase, with the latter two being grouped together as advanced phase. In some cases categorisation can be difficult and there are various criteria for defining the three phases of CML.

The majority of patients are diagnosed in the chronic phase. The course of the chronic phase is initially stable with most patients remaining responsive to treatment. After around 3-5 years about two-thirds of patients experience a transition into the accelerated phase or blast crisis. The accelerated phase is a poorly defined period, typically lasting between 2-15 months and is frequently marked by difficulty in controlling white blood cell counts with standard doses of chemotherapy. Approximately one-third of patients with CML progress to blast crisis, without entering the accelerated phase. Blast crisis generally lasts for between 3-6 months and is a terminal stage in which the disease transforms into a fatal acute leukaemia. It is also relatively refractory to cytotoxic treatment.

Most people with CML (95%) have a chromosomal abnormality commonly known as the 'Philadelphia chromosome'. This is a reciprocal translocation between parts of the long arms of chromosome 22 and chromosome 9, and is associated with fusion of the BCR and ABL genes and the production of a deregulated tyrosine kinase oncoprotein.

CML is a rare disease with an incidence of 1 or 2 cases per 100 000 people every year. It accounts for about one in six leukaemias in adults. It is most common in older people, with a median age at diagnosis of around 65 years. In 2004 there were 492 new cases of CML diagnosed in England and Wales, and 200 registered deaths. It has been estimated that approximately 2,600 people in England and Wales have CML.

For first line treatment of newly diagnosed CML in the chronic phase the tyrosine kinase inhibitor imatinib is recommended (NICE TA 70). Chemotherapy with hydroxycarbamide or busulfan may also be used. Allogenic stem cell transplant is suitable for some patients. Interferon-alfa is a further option which is usually considered after the failure of first line treatment.

The technology

Nilotinib (Tasigna, Novartis) is an oral tyrosine kinase inhibitor which works by selective inhibition of signal transduction associated with the BCR-ABL oncoproteins. This reduces the uncontrolled growth of leukaemia cells.

Nilotinib does not currently hold a marketing authorisation for the first line treatment of CML. It has been studied in clinical trials compared with imatinib in adults with newly diagnosed, Philadelphia chromosome positive, chronic phase CML.

Nilotinib has a marketing authorisation for the treatment of adults with chronic phase and accelerated phase Philadelphia chromosome positive chronic myelogenous leukaemia with resistance or intolerance to prior therapy including imatinib.

Intervention(s)	Nilotinib
Population(s)	Newly diagnosed adult patients with Philadelphia chromosome positive chronic myeloid leukaemia in chronic phase.
Standard comparators	<ul style="list-style-type: none"> ▪ Imatinib ▪ Chemotherapy such as hydroxycarbamide or busulfan
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> ▪ overall survival ▪ progression-free survival ▪ response rates ▪ adverse effects of treatment ▪ health-related quality of life.

Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p>
Other considerations	<p>Guidance will only be issued in accordance with the marketing authorisation.</p>
Related NICE recommendations	<p>Related Technology Appraisals:</p> <p>Technology Appraisal No.70, October 2003, 'Guidance on the use of imatinib for chronic myeloid leukaemia'.</p> <p>Technology Appraisal in Preparation, 'Nilotinib and dasatinib for imatinib-resistant or intolerant chronic myeloid leukaemia'. Earliest anticipated date of publication: tbc</p> <p>Related Guidelines:</p> <p>Cancer Service Guidance, October 2003, Improving outcomes in haematological cancers.</p>

Questions for consultation

Have the most appropriate comparators for the first line treatment of CML been included in the scope? Are the comparators listed routinely used in clinical practice? Is allogenic stem cell transplantation an appropriate comparator for nilotinib?

Are there any subgroups of patients in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Are there any issues that require special attention in light of the duty to have due regard to the need to eliminate unlawful discrimination and promote equality?

Which process would be the most suitable for appraising this technology, the single technology or multiple technology process? Would it be appropriate to combine the appraisal of nilotinib for first line treatment of CML with a review of imatinib for the same indication?

(Information on these processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)