NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Multiple Technology Appraisal

Dasatinib, nilotinib and standard-dose imatinib for the first-line treatment of chronic myeloid leukaemia (including part-review of NICE technology appraisal guidance 70)

Scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of dasatinib, nilotinib and standard-dose imatinib within their licensed indications for the first-line treatment of chronic myeloid leukaemia (including part-review of TA70).

Background

Chronic myeloid leukaemia (CML) is characterised by the production of an excessive number of white cell precursors by the bone marrow. CML progresses slowly through 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 people are diagnosed in the chronic phase. The course of the chronic phase is initially stable with most people remaining responsive to treatment; around 60% of people will remain in chronic phase and in complete cytogenic remission for at least 5 years. From the chronic phase, people with CML either go through the accelerated phase or move straight into blast crisis. The accelerated phase is a poorly defined period. Blast crisis generally lasts for between 3-6 months and is a terminal stage in which the disease transforms into a fatal acute leukaemia.

Ninety-five percent of people with CML have a specific chromosomal abnormality commonly known as the 'Philadelphia chromosome'. This is caused by an exchange of genetic material between two chromosomes (known as reciprocal translocation); between parts of the long arms of chromosome 22 and chromosome 9. It is associated with fusion of the breakpoint cluster region (BCR) and Abelson (ABL) genes and the production of an abnormal tyrosine kinase oncoprotein. BCR-ABL is the only known cause of CML.

CML is a rare disease with an incidence of approximately 1 per 100,000 people every year. It accounts for about one in six cases of leukaemia in adults. Approximately 600 to 800 people are diagnosed with CML in England

and Wales each year. It has been estimated that median life expectancy is at least 15 years. The median age at diagnosis is between 50 and 60 years.

NICE technology appraisal guidance 70 recommends imatinib as first-line treatment for people with Philadelphia-chromosome-positive CML in the chronic phase. NICE is currently appraising dasatinib and nilotinib for imatinib-intolerant CML. An appraisal of dasatinib, nilotinib and high-dose imatinib for imatinib-resistant CML (part-review of TA70) is also underway.

The technologies

Dasatinib (Sprycel, Bristol Myers Squibb), nilotinib (Tasigna, Novartis Pharmaceuticals) and imatinib (Glivec, Novartis Pharmaceuticals) are oral tyrosine kinase inhibitors (TKIs). These particular TKIs work by blocking specific signals in cells expressing the BCR-ABL protein, which reduces the uncontrolled proliferation of white blood cells. Imatinib and nilotinib have a high specificity for the BCR-ABL protein, whilst dasatinib acts on multiple targets. Dasatinib, nilotinib and imatinib are administered orally.

Dasatinib has a UK marketing authorisation for the treatment of adult patients with newly diagnosed Philadelphia chromosome positive CML in the chronic phase. Nilotinib has a UK marketing authorisation for the treatment of adult patients with newly diagnosed Philadelphia chromosome positive CML in the chronic phase. Imatinib has a UK marketing authorisation for use in adult and paediatric patients with newly diagnosed Philadelphia chromosome (bcr-abl) positive CML for whom bone marrow transplantation is not considered as the first-line of treatment. The recommended starting dosage of imatinib is 400mg/day for patients in chronic phase CML.

Intervention(s)	• Dasatinib • Nilotinib • Standard-dose imatinib (400mg daily)
Population(s)	Adults with newly diagnosed Philadelphia chromosome positive chronic myeloid leukaemia in the chronic phase.
Comparators	The interventions will be compared with each other, in line with their marketing authorisations.

Outcomes	The outcome measures to be considered include: • event-free survival • progression-free survival • time to progression • overall survival • response rates – cytogenetic, molecular and haematological • time to treatment failure • adverse effects of treatment • health-related quality of life
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. 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. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. If evidence allows, the appraisal will consider subgroups based on people with and without genetic mutations.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No.70, October 2003, 'Guidance on the use of imatinib for chronic myeloid leukaemia'. Technology Appraisal in preparation, 'Dasatinib and nilotinib for imatinib-intolerant chronic myeloid leukaemia.' Expected publication date: tbc. Technology Appraisal in preparation, 'Dasatinib, nilotinib and high dose imatinib for imatinib-resistant chronic myeloid leukaemia'. (Part-review of TA70). Expected publication date: September 2011. Related Guidelines: Cancer Service Guidance, October 2003, Improving outcomes in haematological cancers.