NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

Bosutinib for previously treated chronic myeloid leukaemia

Final scope

Remit/appraisal objective

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

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. From the chronic phase, people with CML either go through the accelerated phase or move straight into blast crisis 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. This translocation is associated with fusion of the breakpoint cluster region (BCR) and Abelson (ABL) genes and leads to the production of an abnormal tyrosine kinase oncoprotein. The BCR-ABL gene fusion and associated abnormal tyrosine kinase 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 diagnoses of leukaemia in adults. Approximately 600 to 800 people are diagnosed with CML in England and Wales each year. The median age at diagnosis is between 50 and 60 years.

NICE technology appraisal guidance 241 (including a part-review of TA70) recommends nilotinib (with a patient access scheme) as second line treatment for people with chronic or accelerated phase Philadelphia-chromosome-positive CML whose CML is resistant to treatment with standard dose imatinib or who have imatinib intolerance. Dasatinib and high-dose imatinib are not recommended for the treatment of chronic, accelerated or

blast-crisis phase Philadelphia-chromosome-positive CML that is resistant to standard-dose imatinib. Other treatment options in clinical practice can include interferon alfa, hydroxycarbamide, bone marrow stem cell transplantation (depending on the availability of a suitable donor) or best supportive care.

The technology

Bosutinib (Bosulif, Pfizer) is a tyrosine kinase inhibitor (TKI) that has a high activity against Src and Abl kinases. This TKI works by blocking specific signals in cells expressing the BCR-ABL protein, which reduces the uncontrolled proliferation of white blood cells. Bosutinib is administered orally.

Bosutinib does not have a UK marketing authorisation for the treatment of CML. It is being studied in a clinical trial in adults with chronic phase Philadelphia-positive CML, whose CML is resistant or intolerant to treatment with imatinib alone (second line) or to imatinib followed by nilotinib or dasatanib (third line).

Intervention(s)	Bosutinib
Population(s)	Adults with previously treated chronic, accelerated or blast phase Philadelphia-chromosome-positive chronic myeloid leukaemia.
Comparators	• Allogeneic stem cell transplantation (with or without leukaemia-style chemotherapy depending on phase of CML) • Hydroxycarbamide • Interferon alfa • Best supportive care
Outcomes	The outcome measures to be considered include: • overall survival • event-free survival • progression-free survival • time to progression • response rates: cytogenetic, haematological and molecular, including time to response and duration of response • 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.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No.251, April 2012. 'Dasatinib, nilotinib and standard-dose imatinib for the first-line treatment of chronic myeloid leukaemia (part review of technology appraisal guidance 70)'. Review date May 2014 Technology Appraisal No. 241, January 2012. 'Dasatinib, high-dose imatinib and nilotinib for the treatment of imatinib-resistant chronic myeloid leukaemia (part review TA70) and dasatinib and nilotinib for people with chronic myeloid leukaemia for whom treatment with imatinib has failed because of intolerance. Review date September 2014. Technology Appraisal No.70, October 2003, 'Guidance on the use of imatinib for chronic myeloid leukaemia'. Related Guidelines: Cancer Service Guidance, October 2003, Improving outcomes in haematological cancers.