NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Dasatinib for acute lymphoblastic leukaemia

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of dasatinib, within its licensed indications, for acute lymphoblastic leukaemia

Background

Acute lymphoblastic leukaemia (ALL) is a cancer that affects lymphocytes and lymphocyte-producing cells. Lymphocytes are white blood cells that produce antibodies and are vital for the body's immune system. In ALL there is an excess production of immature lymphocyte-precursor cells called blast cells in the bone marrow. Eventually, the production of normal blood cells is affected by this and there is a reduction in the numbers of red cells, white cells and platelets in the blood.

ALL is the only form of leukaemia that is commonest in childhood (under 15 years of age). ALL occurs more frequently between the ages of 15 to 25 and in those over 75 years compared with other age groups. Estimates for the incidence of ALL in the UK ranges from 200 to approximately 600 per year. In 2003, 253 people died of ALL in England and Wales.

Estimates suggest that 20-30% of adults with ALL 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. This results in the fusion of the BCL and ABL genes and the production of a deregulated tyrosine kinase oncoprotein. Prevalence of Philadelphia chromosome positive (Ph+) ALL in adults increases with age and adults with Ph+ ALL have poor prognosis with less than 10% 5-year survival rate.

The aim of treatment in ALL is to achieve a cure. First line treatment of newly diagnosed Ph+ ALL is with a variety of combination chemotherapies, commonly with imatinib. Younger patients with compatible donors are candidates for allogenic bone marrow transplants. Imatinib is also used for consolidation or maintenance therapy. Resistance to imatinib may develop and therapeutic options following resistance to imatinib are limited.

The technology

Dasatinib [Sprycel, Bristol Myers Squibb] is a signal transduction BCR/ABL tyrosine kinase inhibitor. This reduces the uncontrolled growth of leukaemia

cells. Dasatinib targets the same enzyme as imatinib but, due to its increased binding affinity, can act on imatinib resistant BCR/ABL mutations.

Dasatinib has a marketing authorisation in the UK for the treatment of adults with Ph+ ALL with resistance or intolerance to prior therapy.

Intervention(s)	Dasatinib
Population(s)	Adults with Philadelphia chromosome positive acute lymphoblastic leukaemia which is resistant to or who are intolerant of prior therapy
Standard comparators	• Imatinib • Allogenic Bone Marrow Transplant • Chemotherapy • Best Supportive Care
Outcomes	The outcome measures to be considered include: • treatment response rates (including cytogenetic and haematologic responses) • time to and duration of response • progression-free survival • overall survival • 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 time horizon for the economic evaluation should reflect the period over which costs and benefits can reasonably be expected given the natural and clinical history of the disease 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 for the technology If the evidence allows, the cost and benefit of analysis for mutations known to be resistant to imatinib and dasatinib should be considered.

Related NICE recommendations	Related Technology Appraisals: None Related Guidelines: Cancer Service Guidance, October 2003, Improving outcomes in haemato-oncology cancer