

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Dasatinib for acute lymphoblastic leukaemia

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of dasatinib for acute lymphoblastic leukaemia

Background

Acute lymphoblastic leukaemia (ALL) is a form of cancer that affects lymphocytes and lymphocyte-producing cells in the bone marrow. Lymphocytes are white blood cells that produce antibodies and are vital for the body's immune system. In ALL there is an accumulation 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). Adult ALL is most common between the ages of 15 to 25 and in those over 75 years. 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 people 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 and is associated with mutations in the BCL and ABL signal transduction genes. 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.

First line treatment of newly diagnosed Ph+ ALL is with either combination therapy including cyclophosphamide, vincristine, adriamycin, and dexamethasone (hyper-CVAD) or with imatinib. Imatinib based regimens are also used for consolidation or maintenance therapy. Expert opinion suggests that over 90% of ALL patients become resistant to imatinib. 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

National Institute for Health and Clinical Excellence

Consultation on the draft scope and provisional matrix for the appraisal of dasatinib for acute lymphoblastic leukaemia

Issue date: December 2007

binding affinity, can act on imatinib resistant BCR/ABL mutations. Dasatinib also targets other signalling pathways including other proto-oncogenic tyrosine kinases which may be a risk factor for imatinib resistance.

Dasatinib has a marketing authorisation for the treatment of adults with Philadelphia chromosome positive (Ph+) acute lymphoblastic leukaemia (ALL) with resistance or intolerance to prior therapy.

Intervention(s)	Dasatinib
Population(s)	People with Philadelphia chromosome positive (Ph+) acute lymphoblastic leukaemia who are resistant or intolerant to prior therapy
Standard comparators	No active treatment
Outcomes	The outcome measures to be considered include: <ul style="list-style-type: none"> • 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 technologies If evidence allows subgroups of patient populations in whom the technologies are clinically effective and cost effective should be considered

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

Questions for consultation

Are there any groups in whom dasatinib is expected to be more clinically or cost-effective or other groups that should be examined separately?

What are the appropriate comparators for dasatinib in this appraisal?

What are the current arrangements for testing for the presence of the Philadelphia chromosome?

Will dasatinib be used alone or in combination with other chemotherapeutic agents?