NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

Health Technology Appraisal

Imatinib for the treatment of unresectable and/or metastatic gastrointestinal stromal tumours (part review of Technology Appraisal No. 86)

Final scope

Appraisal objective

To appraise the clinical and cost effectiveness of imatinib within its licensed indication for the treatment of unresectable and/or metastatic gastrointestinal stromal tumours which have progressed on treatment at a dose of 400 mg/day.[1]

Background

Gastrointestinal stromal tumours (GISTs) are rare connective tissue tumours. Although GISTs can occur along the length of the GI tract, the majority arise in the stomach (60–70%). GISTs can also occur in the small bowel (25–35%), colon and rectum (5%) and, to a lesser extent, the oesophagus. Most GISTs are associated with the over-expression of the marker KIT (CD117), a tyrosine kinase receptor, which is thought to promote tumour growth or to inhibit tumour cell death via a signal transduction pathway. Many people with GISTs are asymptomatic during early stages of the disease until tumours reach a large size, at which time the tumours can rupture and bleed or obstruct the GI tract.

As a result of difficulties in the diagnosis of GIST, estimates of its incidence vary widely. Based on figures from the manufacturers of imatinib, the number of new cases of unresectable and/or metastatic GISTs is estimated to be less than 240 per year in England and Wales. Although GISTs can occur at any age, the mean age of presentation is between 50 and 70 years and it is more common in men than women. Few people with unresectable and/or metastatic GISTs survive beyond 5 years unless treated.

Current NICE guidance (TA 86) recommends imatinib at a dose of 400 mg/day for the first-line management of people with KIT (CD117)-positive, unresectable and/or metastatic GISTs. Approximately 16% of patients will experience primary resistance to imatinib, and most patients will develop a reduced response at a later stage. TA 86 recommends continuation with imatinib therapy only if a response to initial treatment is achieved within 12 weeks, and continuation of treatment is recommended at a dose of 400 mg/day until the tumour ceases to respond. An

[1] The original remit from the Department of Health/National Assembly for Wales was "To appraise the clinical and cost effectiveness of imatinib in its licensed indication for the treatment of gastro-intestinal stromal tumours"

increase in the dose of imatinib is not recommended in TA 86 for those who develop progressive disease after initially responding. Once imatinib treatment has failed and in the absence of further treatment, survival is usually less than 1 year. A Final Appraisal determination (FAD) for the NICE technology appraisal of sunitinib for the treatment of people with unresectable and/or metastatic malignant GIST has been issued.

The technology

Imatinib (Glivec, Novartis Pharmaceuticals) is a selective kinase inhibitor. Imatinib inhibits proliferation and induces apoptosis in GISTs over-expressing CD117; this is thought to inhibit tumour growth or to promote tumour cell death via a signal transduction pathway.

Imatinib has a UK marketing authorisation for the treatment of adult patients with KIT (CD 117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumours. The recommended dose of imatinib is 400 mg/day for patients with unresectable and/or metastatic malignant GIST but the summary of product characteristics allows for the dose to be increased to 600 mg or 800 mg in patients whose disease progresses at the lower (400 mg) dose. Imatinib is administered orally.

Intervention	Imatinib at escalated doses of 600 mg/day or 800 mg/day
Population	People with KIT (CD 117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumours (GIST) whose disease has progressed on treatment with imatinib at a dose of 400 mg/day
Comparators	• sunitinib • best supportive care
Outcomes	• overall survival • disease-free survival • adverse effects of treatment • health-related quality of life • progression-free survival • time to treatment failure • overall response

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, subgroup analysis by mutational type will be considered and any costs associated with subtyping should be included in the economic analysis.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 86, October 2004, Imatinib for the treatment of unresectable and/or metastatic gastrointestinal stromal tumours. Technology Appraisal in development, Sunitinib malate for the treatment of gastrointestinal stromal tumours (earliest anticipated date of publication September 2009)