NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

Sunitinib for the treatment of gastrointestinal stromal tumours

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of sunitinib within its licensed indication for the treatment of unresectable and/or metastatic malignant gastrointestinal stromal tumours.

Background

Gastro-intestinal 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 around 240 people per year. 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. The prognosis for people with unresectable and/or metastatic GISTs is poor, unless treated, with few people surviving beyond 5 years.

For people with unresectable and/or metastatic GISTs, the current NICE guidance states that imatinib is recommended as a first-line treatment. A review of this guidance has recently been proposed. Approximately 30-50 patients will experience primary resistance to imatinib, and around 60-100 patients would develop a reduced response at a later stage. There is no current guidance for people with unresectable and/or metastatic GISTs who have failed imatinib treatment due to resistance or intolerance, and these patients are offered symptom relief and best supportive care. Best supportive care could comprise of radiofrequency ablation of the tumour, stenting, embolisation and laser endoscopy. Following failed imatinib treatment and in the absence of further treatment, survival is usually less than 1 year.

The technology

Sunitinib (Sutent, Pfizer Limited) is a multi-targeted tyrosine kinase inhibitor. It is a non-specific inhibitor of the platelet-derived growth factor receptor (PDGFR), vascular endothelial growth factor receptor (VEGFR), KIT and foetal liver tyrosine kinase 3 receptors on endothelial, pericytes and cancer cells. In doing this, sunitinib promotes anti-tumour and anti-angiogenic activity, leading to cancer cell death.

Sunitinib has a marketing authorisation for the treatment of unresectable and/or metastatic malignant GISTs after failure of imatinib treatment due to resistance or intolerance. Sunitinib is administered orally.

Intervention(s)	Sunitinib
Population(s)	People with unresectable and/or metastatic GISTs after failure of imatinib due to resistance or intolerance.
Standard comparators	Best supportive care
Outcomes	• overall survival • progression-free survival • response rates • 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	Details of the components of best supportive care should be clearly described. Guidance will only be issued in accordance with the marketing authorisation.

Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 86, October 2004, Imatinib for the treatment of unresectable and/or metastatic gastrointestinal stromal tumours (review proposed).