NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Regorafenib for the treatment of metastatic colorectal cancer following prior treatment for metastatic disease

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of regorafenib within its licensed indication for the treatment of metastatic colorectal cancer that has progressed following prior treatment for metastatic disease.

Background

Colorectal cancer is a malignant neoplasm arising from the lining of the large intestine (colon and rectum). In 2009 more than 41,000 people were diagnosed with colorectal cancer in the UK and approximately 16,000 people died of colorectal cancer in the UK in 2010. Occurrence of colorectal cancer increases with age, with more than 8 in 10 cases occurring in people aged 60 and over. The median age of patients at diagnosis is over 70 years.

In metastatic colorectal cancer the tumour has spread beyond the confines of the lymph nodes to other parts of the body. Between 20–55% of people first diagnosed with colorectal cancer have metastatic disease. In addition, approximately 50–60% of patients who have undergone surgery for early stage colorectal cancer with apparently complete excision will eventually develop advanced disease and distant metastases (typically presenting within 2 years of initial diagnosis). The 5-year survival rate for metastatic colorectal disease is 6.6%.

The management of metastatic colorectal cancer is mainly palliative and involves a combination of specialist treatments (such as palliative surgery, chemotherapy and radiation), symptom control and psychosocial support.

NICE clinical guideline no. 131 recommends the following sequences of chemotherapy for people with metastatic colorectal cancer: folinic acid plus fluorouracil plus oxaliplatin (FOLFOX) as first line treatment then single agent irinotecan as second-line treatment, or FOLFOX as first-line treatment then folinic acid plus fluorouracil plus irinotecan (FOLFIRI) as second-line treatment, or capecitabine plus oxaliplatin (XELOX) as first-line treatment then FOLFIRI as second-line treatment. For people who are intolerant to 5-fluorouracil and folinic acid, or for whom these drugs are not suitable, raltitrexed may be considered. NICE has not recommended treatment with bevacizumab in combination with fluoropyrimidine-based chemotherapy, cetuximab chemotherapy or monotherapy, and panitumumab monotherapy for metastatic colorectal cancer that has progressed following first-line treatment with chemotherapy (NICE Technology Appraisal No.242). NICE was unable to

recommend the use in the NHS of panitumumab in combination with FOLFIRI for the treatment of metastatic colorectal cancer that has progressed following first-line treatment with chemotherapy because no evidence submission was received from the manufacturer or sponsor of the technology.

The technology

Regorafenib (Stivarga, Bayer) inhibits angiogenic kinase receptors, such as the vascular endothelial growth factor and the TIE2 receptor, which play a role in angiogenesis. It also inhibits oncogenic kinases such as RAF, RET and c-KIT, thereby preventing the proliferation of cancer cells. It is administered orally.

Regorafenib does not have a UK marketing authorisation for the treatment of metastatic colorectal cancer. It has been studied in clinical trials compared with placebo for the treatment of people with metastatic colorectal cancer whose disease has progressed after standard therapies including a fluoropyrimidine, oxaliplatin, irinotecan, bevacizumab; and cetuximab or panitumumab for patients who had *KRAS* wild-type tumours.

Intervention(s)	Regorafenib
Population(s)	People with metastatic colorectal cancer whose disease has progressed following prior treatment for metastatic disease.
Comparators	Best supportive care
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • 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. 242, Jan 2012, 'Cetuximab (monotherapy or combination chemotherapy), bevacizumab (in combination with non-oxaliplatin chemotherapy) and panitumumab (monotherapy) for the treatment of metastatic colorectal cancer after first-line chemotherapy (review of TA150 and part review of TA118)' Review decision date Jan 2015 Terminated Technology Appraisal No. 240, Dec 2011, 'Panitumumab in combination with chemotherapy for the treatment of metastatic colorectal cancer' Technology Appraisal in Preparation, 'Aflibercept for the treatment of metastatic colorectal cancer which has progressed following prior oxaliplatin-based chemotherapy' Earliest anticipated date of publication Oct 2013 Related Guidelines: Clinical Guideline No. 131, Nov 2011, 'Colorectal cancer: The diagnosis and management of colorectal cancer' Related Quality Standards Quality Standard No. 20, Aug 2012, 'Colorectal cancer quality standard'