NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Aflibercept in combination with irinotecan and fluorouracil-based therapy for the treatment of metastatic colorectal cancer which has progressed following prior oxaliplatin-based chemotherapy

Final Scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of aflibercept in combination with irinotecan and fluorouracil-based therapy within its licensed indication for the treatment of metastatic colorectal cancer which has progressed following prior oxaliplatin-based chemotherapy.

Background

Colorectal cancer is a malignant tumour arising from the lining of the large intestine (colon and rectum). In 2007 there were approximately 34,000 people diagnosed with colorectal cancer and 14,000 deaths in England and Wales. Incidence of colorectal cancer increases with age, with almost three-quarters of diagnoses occurring in people older than 65 years.

In metastatic colorectal cancer the tumour has spread beyond the confines of the lymph nodes to other parts of the body. Between 20% and 55% of people first diagnosed with colorectal cancer have metastatic disease. In addition, approximately 50 to 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%.

People who have metastatic colorectal cancer receive a combination of specialist treatments (such as surgery, chemotherapy and radiation), symptom control and psychosocial support.

NICE clinical guideline 131 recommends oxaliplatin in combination with infusional fluorouracil plus folinic acid (FOLFOX) or capecitabine plus oxaliplatin (XELOX) as first-line treatment options for metastatic colorectal cancer. Following FOLFOX, single agent irinotecan alone or folinic acid in combination with infusional fluorouracil and irinotecan (FOLFIRI) are recommended as second-line treatment options.

The technology

Aflibercept (VEGF-Trap, Sanofi and Regeneron Pharmaceuticals) is a recombinant fusion protein that binds to vascular endothelial growth factor- A and B (VEGF-A, VEGF-B), and Placental Growth Factor isoforms (PLGF1, PLGF2), thereby preventing the growth of new capillary blood vessels. This reduces vascularisation of tumours and inhibits tumour growth. Aflibercept is administered by intravenous infusion.

Aflibercept does not have a marketing authorisation in the UK for the treatment of metastatic colorectal cancer. In November 2012, the Committee for Medicinal Products for Human Use of the European Medicines Agency (CHMP) recommended the approval of aflibercept for use in combination with irinotecan/5-fluorouacil/folinic acid (FOLFIRI) chemotherapy for the treatment of adults with metastatic colorectal cancer that is resistant to or has progressed after an oxaliplatin-containing regimen.

Intervention(s)	Aflibercept in combination with irinotecan and fluorouracil-based therapy
Population(s)	People with metastatic colorectal cancer that is resistant to or has progressed following prior oxaliplatin based chemotherapy.
Comparators	Irinotecan in combination with fluorouracil-based therapy
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, January 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'. This guidance replaces Technology Appraisal No. 150. Technology Appraisal, No. 118, January 2007, Bevacizumab and cetuximab for the treatment of metastatic colorectal cancer. This guidance is partially updated by Technology Appraisal No. 242. Technology Appraisal No. 61, May 2003, Capecitabine and tegafur uracil for metastatic colorectal cancer. Moved to static list in April 2006. Technology Appraisal No. 212, December 2010, Bevacizumab in combination with oxaliplatin and either 5-fluorouracil plus folinic acid or capecitabine for the treatment of metastatic colorectal cancer. Review date: May 2013. Technology Appraisal No. 240, December 2011, 'Panitumumab in combination with chemotherapy for the treatment of metastatic colorectal cancer (terminated appraisal)'. Related Guidelines: Guidance on Cancer Services, June 2004, Improving outcomes in colorectal cancer. Clinical Guideline No.131, November 2011, 'Colorectal cancer: the diagnosis and management of colorectal cancer'. This guideline replaces Technology Appraisal No. 93.