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

Draft scope (Pre-referral)

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 neoplasm 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. Occurrence of colorectal cancer increases with age, with 83% of cases arising in people older than 60 years. 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% 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 12%.

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

NICE technology appraisal No. 93 recommends oxaliplatin in combination with infusional fluorouracil plus folinic acid (FOLFOX) and irinotecan in combination with infusional fluorouracil plus folinic acid (FOLFIRI) as first-line treatment options for metastatic colorectal cancer. The oral analogues of fluorouracil, capecitabine , with tegafur-uracil (and folinic acid) are also recommended as first-line treatment options for metastatic colorectal cancer (technology appraisal No. 61). FOLFOX or irinotecan alone are recommended as subsequent therapy options (technology appraisal No. 93).

The technology

Aflibercept (VEGF-Trap, Sanofi and Regeneron Pharmaceuticals) is a fully human recombinant fusion protein. Aflibercept binds to all vascular endothelial growth factor-A isoforms thereby preventing the growth of new capillary blood vessels. This reduces vascularisation of tumours and inhibits tumour growth. It is administered by intravenous infusion.

Aflibercept does not have a marketing authorisation in the UK for the treatment of metastatic colorectal cancer. It is being studied in combination with FOLFIRI in clinical trials of people with inoperable metastatic colorectal cancer that has failed to respond to prior oxaliplatin-based chemotherapy, compared with placebo in combination with FOLFIRI.

Intervention(s)	Aflibercept in combination with irinotecan and fluorouracil-based therapy
Population(s)	People with metastatic colorectal cancer that has progressed following prior oxaliplatin based chemotherapy.
Comparators	• irinotecan in combination with fluorouracil-based therapy • irinotecan alone
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. 93, August 2005 (review of TA33). Irinotecan, oxaliplatin and raltitrexed for advanced colorectal cancer. Currently being incorporated in an on-going clinical guideline, "Diagnosis and management of colorectal cancer". Expected date of publication October 2011. Technology Appraisal, No. 150, June 2008, Cetuximab for the treatment of metastatic colorectal cancer following failure of oxaliplatin-containing chemotherapy (terminated appraisal). Under review. Technology Appraisal, No. 118, January 2007, Bevacizumab and cetuximab for the treatment of metastatic colorectal cancer. Under review. 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. Technology Appraisal in Preparation, Panitumumab in combination with chemotherapy within its licensed indication for the treatment of metastatic colorectal cancer. Earliest anticipated date of publication TBC. Technology Appraisal in Preparation, 'Cetuximab (mono- or combination chemotherapy) bevacizumab (combination with non-oxaliplatin chemotherapy) and panitumumab (monotherapy) for the treatment of metastatic colorectal cancer after first-line chemotherapy (review of technology appraisal 150 and part-review of technology appraisal 118)'. Earliest anticipated date of publication TBC. Related Guidelines: Guidance on Cancer Services, June 2004, Improving outcomes in colorectal cancer. Clinical Guideline in Preparation, Diagnosis and management of colorectal cancer. Earliest anticipated

	date for publication, October 2011.

Questions for consultation

Have the most appropriate comparators for aflibercept been included in the scope? Are there any other comparators routinely used in clinical practice?

Will the intervention be given only in combination with irinotecan?

Are there any subgroups of people in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Are there any issues that require special attention in light of the duty to have due regard to the need to eliminate unlawful discrimination and promote equality?

Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)