NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Bevacizumab in combination with oxaliplatin and either 5FU or capecitabine for the treatment of metastatic colorectal cancer

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of bevacizumab within its licensed indication in combination with oxaliplatin and either 5FU or capecitabine for the treatment of metastatic colorectal cancer.

Background

Colorectal cancer is a malignant neoplasm arising from the lining (mucosa) of the large intestine (colon and rectum). Colorectal cancer is the third most common cancer in the UK, with approximately 30,000 new cases diagnosed in England and Wales in 2004, and approximately 14,000 deaths registered in 2005. This represents 12% of all new cancer cases in women and 14% of all new cancer cases in men. In people between the ages of 45 and 49 years the incidence is 20 per 100,000. Amongst those over 75 years of age, the incidence is over 300 per 100,000 for men and 200 per 100,000 per year for women. The median age of patients at diagnosis is over 70 years.

In metastatic colorectal cancer the tumour has spread beyond the confines of the locoregional lymph nodes to other parts of the body. This is described as stage IV of the American Joint Committee on Cancer (AJCC) tumour node metastases (TNM) system or stage D of Dukes' classification. Estimates of people presenting with metastatic colorectal cancer range from 20% to 55% of new cases. In addition, out of patients who have undergone surgery for early stage colorectal cancer with apparently complete excision, approximately 50-60% 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 palliative surgery, chemotherapy and radiation), symptom control and psychosocial support. However, approximately 20% of patients with metastatic colorectal cancer present with potentially resectable liver metastases. In addition, estimates suggest that for between 10% and 50% of patients chemotherapy may render unresectable liver metastases operable. The resection of metastases can result in longer term survival for a proportion of patients.

Current guidance from NICE recommends infusional 5-fluorouracil plus folinic acid (5-FU/FA), oxaliplatin plus infusional 5 FU/FA (FOLFOX), and irinotecan plus infusional 5-FU/FA (FOLFIRI) as first line treatment options (technology appraisal 93). The oral analogues of 5-FU capecitabine and tegafur with uracil are also recommended as treatment options (technology appraisal 61). Bevacizumab as a first line treatment in combination with 5-FU plus folinic acid, with or without irinotecan is not recommended as a treatment option (technology appraisal 118).

The technology

Bevacizumab (Avastin, Roche Products) is a recombinant humanised monoclonal IgG1 antibody that acts as an angiogenesis inhibitor by targeting the biologic activity of human vascular endothelial growth factor (VEGF), which stimulates new blood vessel formation in the tumour.

Bevacizumab was licensed in January 2005 for the first-line treatment of metastatic carcinoma of the colon or rectum in combination with intravenous 5-fluorouracil/folinic acid with or without irinotecan. In January 2008, bevacizumab received a licence extension, which allows it to be combined with any fluoropyrimidine-based chemotherapy for the treatment of metastatic colorectal cancer. The marketing authorisation does not specify a line of treatment.

Intervention(s)	Bevacizumab in combination with oxaliplatin and either 5-FU or capecitabine
Population(s)	People with metastatic colorectal cancer for whom oxaliplatin-including chemotherapy regimens are suitable
Standard comparators	• oxaliplatin-including chemotherapy regimens without bevacizumab • irinotecan-including chemotherapy regimens without bevacizumab

Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • resection rates of metastases • 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. If evidence allows the appraisal should consider the following subgroup: • patients for whom metastases may become resectable following chemotherapy If evidence allows the appraisal should consider the use of continuation rules based on tumour response, or another appropriate clinical marker.

Related NICE recommendations	Related Technology Appraisals: Technology Appraisal, No. 118, January 2007. Bevacizumab and cetuximab for the treatment of metastatic colorectal cancer. Technology Appraisal, No. 100, April 2006. Capecitabine and oxaliplatin in the adjuvant treatment of stage III (Dukes' C) colon cancer. Technology Appraisal, No. 93, August 2005. (review of TA33). Irinotecan, oxaliplatin and raltitrexed for advanced colorectal cancer. Technology Appraisal, No. 61, May 2003. Capecitabine and tegafur uracil for metastatic colorectal cancer. Technology Appraisal in Preparation, Cetuximab for the first line treatment of metastatic colorectal cancer. Earliest anticipated date of publication: to be confirmed Technology Appraisal in Preparation, Cetuximab for the treatment of metastatic colorectal cancer following failure of oxaliplatin-containing chemotherapy. Earliest anticipated date of publication: to be confirmed Related Guidelines: Clinical Guideline in Preparation, Diagnosis and management of colorectal and anal cancer. Earliest anticipated date of publication: to be confirmed Guidance on Cancer Services, June 2004, Improving outcomes in colorectal cancers.

Questions for consultation

Have the most appropriate comparators for the treatment of bevacizumab in combination with oxaliplatin and either 5-FU or capecitabine been included in the scope?

- Should 5-fluorouracil plus folinic acid (5-FU/FA) (and oral analogues) be added to the list of comparators?

Are the subgroups suggested in ‘other considerations’ appropriate?

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?

Which process would be the most suitable for appraising this technology, the single technology or multiple technology process? (Information on these

processes is available at
http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)