NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

Health Technology Appraisal

The use of oxaliplatin and capecitabine for the adjuvant treatment of colon cancer

Draft Scope

Objectives:

To appraise the clinical and cost effectiveness of the use of oxaliplatin, and capecitabine, as adjuvant therapies in the treatment of patients with Dukes' stage C colon cancer after complete surgical resection of the primary tumour.[i]

Background:

Colon cancer is a malignant neoplasm arising from the lining (mucosa) of the large intestine. Dukes' staging of colon (and rectal) cancer classifies tumours as stage A (localised within the bowel wall), B (penetrates the bowel wall), C (spread to the regional lymph nodes), or D (distant metastasis). The American Joint Committee on Cancer (or TNM) staging system can also be used. This system looks at how deeply the tumor has penetrated into the bowel wall (T), whether lymph nodes are affected by the cancer (N) and whether metastases are present (M); stage 2 (T3 or T4,N0,M0) is equivalent to Dukes' stage B and stage 3 (any T,N1 or N2,M0) is equivalent to Dukes' stage C.

Current Guidance on Cancer Services recommends that systematic chemotherapy should be offered to all patients who, after surgery for Dukes' stage C colon or rectal cancer, are fit enough to tolerate it. Intravenous 5-fluorouracil and folinic acid (5FU/FA), given intravenously over six months, is seen to be the standard treatment.

In 2000, there were approximately 22,000 new cases of colon cancer diagnosed in England and Wales. Colorectal cancer is the third most common cancer in the UK after breast and lung cancer, with an annual incidence of 60.2 cases per 100,000. The lifetime risk of developing colorectal cancer is 1 in 18 for men and 1 in 20 for women. Colorectal cancer predominantly affects older people and over half of all deaths occur in people older than 75 years of age. Approximately 26% of patients diagnosed with colorectal cancer are classified as Dukes' stage C at presentation.

The technologies:

Oxaliplatin (Eloxatin, Aventis) is an intravenously administered, water soluble, platinum-based cytotoxic compound that cross links DNA, preventing replication and hence cell division. Oxaliplatin is currently licensed for the treatment of metastatic colorectal cancer in combination with 5FU/FA. A Mutual Recognition Procedure in Europe was completed successfully in September 2004 which will result in an extended indication: 'adjuvant treatment of stage III (Dukes' C) colon cancer after complete resection of primary tumour'.

Capecitabine (Xeloda, Roche) is an orally administered, non-cytotoxic fluoropyrimidine carbamate which is a precursor of 5-fluorouracil. Capecitabine is currently licensed for first-line monotherapy of metastatic colorectal cancer. A submission has been made to EMEA to extend the licensed indications to include adjuvant treatment after surgery of patients with Dukes' C colon cancer.

Intervention(s)	• Oxaliplatin (in combination with 5-FU/FA) • Capecitabine
Population(s)	People with Dukes' stage C colon cancer after complete surgical resection of the primary tumour
Current standard treatments (comparators)	Treatment without oxaliplatin or capecitabine to include: • No adjuvant chemotherapy • Adjuvant chemotherapy with established fluorouracil-containing regimen
Other considerations:	The clinical and cost effectiveness of irinotecan as adjuvant therapy in colorectal cancer will be the subject of a separate appraisal (see below). Treatments listed above under 'interventions' can be compared with each other. The interventions will be appraised in accordance with licensed indications. Outcomes should include: • Survival • Progression-free or disease-free survival • Time to treatment failure • Adverse effects of treatment • Health-related quality of life If evidence allows, consideration should be given to different methods of delivering treatment such as bolus injection or continuous infusion.
Related NICE recommendations	**In progress** Technology Appraisal: Review of the clinical effectiveness and cost effectiveness of irinotecan, oxaliplatin and raltitrexed for the treatment of advanced colorectal cancer. Expected date of issue Review August 2005.

	Technology Appraisal: The clinical- and cost-effectiveness of irinotecan as adjuvant therapy in colorectal cancer. Expected date of issue January 2007. **Completed** Guidance on Cancer Services. Improving Outcomes in Colorectal Cancer. Expected date of issue May 2004. Guidance on the use of capecitabine and tegafur with uracil for metastatic colorectal cancer. Technology Appraisal 61. Issued May 2003. Guidance on the use of irinotecan, oxaliplatin and raltitrexed for the treatment of advanced colorectal cancer. Technology Appraisal 33. Issued March 2002.

Irinotecan:
The remit for this appraisal includes consideration of irinotecan as adjuvant therapy in colorectal cancer. The anticipated licensing timescale for irinotecan is not compatible with the scheduling of this appraisal, and it is our intention to consider irinotecan in a separate appraisal. This will allow the current appraisal to proceed as soon as possible. The views of consultees and commentators on this approach are particularly welcome.

[i] The Department of Health remit to the Institute is "To appraise the cost and clinical effectiveness of the use of oxaliplatin, irinotecan and capecitabine as adjuvant therapy in colorectal cancer.