

Oxaliplatin (for metastatic colorectal cancer)

Product:
OXALIPLATIN (Eloxatin®)

Class of drugs:
Antineoplastic

Indication:
Treatment of metastatic colorectal cancer

Manufacturer:
sanofi aventis Canada Inc.

CED Recommendation

For the initial or first-line treatment of metastatic colorectal cancer, the CED recommended that oxaliplatin (Eloxatin) be funded only in patients who have a contraindication or intolerance to the FOLFIRI regimen, on the basis that oxaliplatin (Eloxatin) is similar in efficacy as this comparator regimen but is significantly more expensive.

For the subsequent or second-line treatment of metastatic colorectal cancer in patients who have failed first-line therapy, the CED recommended that oxaliplatin (Eloxatin) not be funded, on the basis that value for money has not been demonstrated in this setting.

Executive Officer Decision

Following the CED's recommendation and based on a subsequent pricing agreement with the manufacturer, the Executive Officer decided to fund oxaliplatin (Eloxatin) for both first- and second-line treatment of metastatic colorectal cancer.

Status

Funding available through Cancer Care Ontario's New Drug Funding Program.

Highlights of Recommendation:

- ◆ Oxaliplatin (Eloxatin) is a chemotherapy agent used in the treatment of colorectal cancer (colon cancer and rectal cancer).
- ◆ This particular review considered the funding of oxaliplatin (Eloxatin) in a combination regimen, called the FOLFOX regimen, for the treatment of metastatic colorectal cancer, which is cancer that has advanced and spread beyond the colon and rectum.
- ◆ The FOLFOX regimen is a combination containing oxaliplatin (Eloxatin) and two other chemotherapy drugs: 5-fluorouracil and leucovorin.
- ◆ An alternative combination treatment for metastatic colorectal cancer is the FOLFIRI regimen. The FOLFIRI regimen combines three chemotherapy drugs: irinotecan, 5-fluorouracil and leucovorin.
- ◆ In the initial or first-line treatment of metastatic colorectal cancer, evidence supports that the FOLFOX regimen and the FOLFIRI regimen provide similar efficacy.
- ◆ However, the two treatment regimens differ in their side effects. The FOLFIRI regimen is associated with a higher risk of low blood cell count and diarrhea. The FOLFOX regimen is associated with a high risk of peripheral neuropathy (pain, numbness, tingling, swelling and muscle weakness in various parts of the body).
- ◆ Because the two regimens have similar efficacy, the difference in side effect profile usually determines which treatment a physician may choose for a particular patient.
- ◆ The FOLFOX regimen is approximately three times more expensive than the FOLFIRI regimen (\$1,492 per treatment cycle versus \$582 per treatment cycle). The Committee indicated that the price premium is not justified.
- ◆ In the subsequent or second-line treatment of metastatic colorectal cancer in patients who have failed first-line treatment, data from one study reported that the FOLFOX regimen provided superior efficacy compared to oxaliplatin (Eloxatin) alone and 5-fluorouracil and leucovorin alone. However, a proper economic evaluation

has not been conducted by the manufacturer to assess value for money in the second-line setting.

- ◆ Overall, the Committee noted that, in the first-line treatment of metastatic colorectal cancer, the FOLFOX regimen is similar in efficacy as the FOLFIRI regimen but is much more expensive. Therefore, the Committee recommended that the FOLFOX regimen be funded for first-line treatment only in patients who have a contraindication or intolerance to the FOLFIRI regimen. The Committee recommended that the FOLFOX regimen not be funded in the second-line treatment of metastatic colorectal cancer because value for money has not been demonstrated.

Background:

Colorectal cancer refers to cancer of the colon (large bowel) and cancer of the rectum. Metastatic colorectal cancer is cancer that has spread to other parts of the body, such as the liver and lung.

Treatment of metastatic colorectal cancer usually consists of combination chemotherapy. For patients unable to tolerate combination therapy, standalone treatments are also available.

Two standard combination regimens for metastatic colorectal cancer are the FOLFIRI regimen (irinotecan, 5-fluorouracil and leucovorin) and the FOLFOX regimen (oxaliplatin, 5-fluorouracil and leucovorin). Standard practice in North America is to choose one of these two regimens as the initial or first-line treatment. If the FOLFIRI regimen is chosen as the first-line treatment and it fails, the patient can be switched to the FOLFOX regimen as their second-line treatment. Likewise, if the FOLFOX regimen fails as first-line treatment, the patient can be switched to the FOLFIRI regimen as their second-line treatment.

continued...

Detailed Discussion:

- ◆ In the first-line treatment of metastatic colorectal cancer, data from three randomized controlled studies (*Goldberg et al. J Clin Oncol 2004. Colucci et al. J Clin Oncol 2005. Tournigand et al. J Clin Oncol 2004.*) support that the FOLFOX regimen and the FOLFIRI regimen provide similar efficacy in measures of overall response rate and median survival.
- ◆ In the Goldberg trial, a median time to progression of 8.7 months, response rate of 45%, and median survival time of 19.5 months were observed with the FOLFOX regimen. These results were superior to those observed with the IFL regimen for all endpoints (6.9 months, 31%, and 15.0 months, respectively). The IFL is a regimen similar to FOLFIRI. With the FOLFIRI regimen, 5-fluorouracil is given by infusion; whereas with IFL, 5-fluorouracil is given by bolus injection. Evidence has shown that infusional 5-fluorouracil is superior to bolus 5-fluorouracil in terms of toxicity and tumor response rate.
- ◆ In the Colucci trial, no significant difference was observed between patients treated with the FOLFOX and the FOLFIRI regimen with respect to overall response rate, median time to progression and overall survival. The overall response rates were 31% in the FOLFIRI group versus 34% in FOLFOX group. In both treatment groups, the median time to progression was 7 months. The overall survival was 14 months versus 15 months, for FOLFIRI and FOLFOX respectively.
- ◆ The Tournigand trial demonstrated similar median survival (21.5 months versus 20.6 months) and overall response rate (56% versus 54%) between the FOLFOX and FOLFIRI regimen.
- ◆ In the second-line treatment of metastatic colorectal cancer, results from one study (*Rothenberg et al. J Clin Oncol 2003*) demonstrated that the FOLFOX regimen provided superior efficacy compared to oxaliplatin (Eloxatin) alone and 5-fluorouracil and leucovorin alone in terms of response rate, time to progression, and symptom control.
- ◆ A meta-analysis (*Grothey et al. J Clin Oncol 2004*) found that patients on first-line combination therapy containing oxaliplatin (e.g. the FOLFOX regimen) should subsequently be offered combination therapy with irinotecan (e.g. the FOLFIRI regimen) as second-line treatment, and vice versa, for maximal survival benefits. The meta-analysis included results from seven randomized controlled trials and found a 3.5 month increase in median survival in patients who received a first-line combination therapy with either oxaliplatin or irinotecan, as compared with patients who received monotherapy.
- ◆ The FOLFOX regimen and the FOLFIRI regimen have different side effect profiles. The FOLFIRI regimen is associated with higher risks of diarrhea and neutropenia, while the FOLFOX regimen is associated with a high risk of peripheral neuropathy.
- ◆ In addition to peripheral neuropathy, other common side effects with the FOLFOX regimen include neutropenia (low white blood cell count), thrombocytopenia (low platelet count), anemia, nausea, diarrhea, vomiting, fatigue, and stomatitis (mouth sores).
- ◆ In terms of costs, the FOLFOX regimen is three times more expensive than the FOLFIRI regimen. The FOLFOX regimen costs \$1,492 per treatment cycle and the FOLFIRI regimen costs \$582 per treatment cycle. Value for money for the FOLFOX regimen has not been demonstrated.
- ◆ Overall, the Committee agreed that available evidence supports the clinical efficacy of the FOLFOX regimen. However, the FOLFOX regimen is significantly more expensive than the FOLFIRI regimen. In the absence of evidence to demonstrate cost-effectiveness, the Committee recommended that the FOLFOX regimen be funded only for the first-line treatment of metastatic colorectal cancer in patients who have a contraindication or intolerance to the FOLFIRI regimen.
- ◆ The CED worked jointly with a subcommittee involving cancer experts to review this cancer drug, as is done for all other cancer drug treatments.

Cancer Care Ontario (CCO) Information:

Information on CCO regimens for colorectal cancer may be found at:

http://www.cancercare.on.ca/index_chemoRegimensbyDisease.htm

The colorectal Disease Site Group Program in Evidence-Based Care Guideline for oxaliplatin (Eloxatin) in colorectal cancer is available at:

<http://www.cancercare.on.ca/english/toolbox/qualityguidelines/diseasesite/gastro-ebc/1>



Ministry of
Health and Long-Term Care
Ontario Public Drug Programs

For more information, please contact:

Ministry of Health and Long-Term Care
Ontario Public Drug Programs

Hepburn Block, 9th Floor
80 Grosvenor Street, Queen's Park
Toronto, Ontario M7A 1R3

or click: http://www.health.gov.on.ca/english/providers/program/drugs/ced_rec_table.html