

Alemtuzumab

Product:

ALEMTUZUMAB (MabCampath®)

Class of drugs:

Antineoplastic agent

Indication:

Treatment of chronic lymphocytic leukemia (CLL)

Manufacturer:

Genzyme Corporation

CED Recommendation

The CED recommended not to fund alemtuzumab (MabCampath) through Cancer Care Ontario's New Drug Funding Program, on the basis that the evidence regarding its effectiveness is weak, and the value-for-money of the drug is unclear.

Executive Officer Decision

Based on the CED's recommendation, the Executive Officer decided not to list alemtuzumab (MabCampath) for the treatment of chronic lymphocytic leukemia (CLL).

Status

No funding through Cancer Care Ontario's New Drug Funding Program.

Highlights of Recommendation:

- ◆ Health Canada has approved alemtuzumab (MabCampath) for the treatment of chronic lymphocytic leukemia (CLL), a cancer that affects the blood.
- ◆ Standard chemotherapy for adult patients with this type of leukemia usually consists of chlorambucil, cyclophosphamide, or fludarabine.
- ◆ Some patients that do not respond to standard chemotherapy appear to respond to alemtuzumab (MabCampath), but there is currently no good evidence from studies that the drug works better than other available treatments.
- ◆ Treatment with alemtuzumab (MabCampath) can cause serious side effects, including severe infections in some patients. Patients must understand both the risk of harm and the chance for benefit. MabCampath costs approximately \$25,000 for one course of therapy. The next most expensive therapy is fludarabine, which costs approximately \$7,200 for each course of therapy.
- ◆ **Overall, the CED noted that the evidence that supports the effectiveness of alemtuzumab (MabCampath) in patients who do not respond to standard chemotherapy is weak, and this medication is associated with severe side effects. In addition, the value-for-money of using alemtuzumab (MabCampath) for the treatment of this form of leukemia is unclear.**
- ◆ The Committee recommended that Cancer Care Ontario's New Drug Funding Program not fund alemtuzumab (MabCampath) for CLL.

Background:

Leukemia is cancer of the body's blood-forming tissues, including the bone marrow and lymphatic system. The disease usually starts in the white blood cells. Chronic lymphocytic leukemia (CLL) is the most common leukemia in Canada. Some patients may live normal life spans without therapy, while others die of the disease within two to three years.

A class of drugs called alkylating agents is used as first-line therapy in most cases. This class includes chemotherapy containing chlorambucil, cyclophosphamide, and fludarabine. If patients have tried and failed the first-line therapy, fludarabine (alone or with other drugs) can be used as a second-line therapy. If patients have tried and failed fludarabine second-line therapy, there is currently no standard third-line treatment.

Alemtuzumab (MabCampath) is used in patients who have been treated with alkylating agents and have failed fludarabine therapy.

Detailed Discussion:

- ◆ Canadian distributor at the time when the submission was received, Berlex Canada Inc., asked the Ministry of Health and Long-Term care to reconsider an earlier decision not to fund alemtuzumab (MabCampath) through Cancer Care Ontario's New Drug Funding Program. (Please note that as of April 18, 2007, Bayer Inc. has become the Canadian distributor for alemtuzumab (MabCampath).)
- ◆ Currently, there are no published randomized controlled trials evaluating alemtuzumab alone or in combination with other chemotherapeutic agents for the treatment of relapsed or refractory CLL.
- ◆ The evidence supporting treatment with alemtuzumab (MabCampath) comes mainly from non-comparative case-series studies that evaluate disease response as the primary outcome measure.

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- ◆ Improvements in quality of life and overall survival from comparative data are not available at this time.
- ◆ Survival data were reported in four single-arm studies evaluating alemtuzumab (MabCampath) in patients with relapsed or refractory disease post-fludarabine. Median overall survival ranged from eight months to more than two years.
- ◆ No studies reported overall survival rates associated with alemtuzumab (MabCampath) therapy for previously untreated patients with CLL.
- ◆ Treatment with alemtuzumab (MabCampath) is associated with significant and potentially serious adverse treatment-related toxicities.
- ◆ The associated Cancer Care Ontario practice guideline noted that there were nine published trials for use of alemtuzumab (MabCampath) in relapsed/refractory patients. A meta-analysis of those trials reported the following hematological toxicities:
 - Grade III/IV neutropenia (22-66%): combined estimate 39%
 - Grade III/IV thrombocytopenia (23-46%): combined estimate 31%
 - Grade III/IV anemia (0-28%): combined estimate 8%
 - Infection related toxicities: all infections 46% (30-93%)
 - Infection-related death: 4.5% (0-10%)
- ◆ Given the potential toxicities associated with alemtuzumab (MabCampath) therapy, use in patients with important co-morbidities may be associated with excessive risks.
- ◆ Berlex Canada Inc. presented a cost-effectiveness analysis. The CED noted that there are many limitations in the analysis.
- ◆ Overall, the CED noted that the clinical efficacy of alemtuzumab (MabCampath) in treating CLL that has not responded to other chemotherapy appears weak, and the toxicities associated with this agent are high. Also, there are limitations in the cost-effectiveness analysis so the CED was unable to determine the value-for-money of this treatment.

Cancer Care Ontario (CCO) Information:

Information on CCO chemotherapy regimens for CLL is available at:

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

The Hematology Disease Site Group (DSG) Program in Evidence-based Care (PEBC) guideline for alemtuzumab (MabCampath) in CLL is available at:

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



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