

Committee to Evaluate Drugs (CED)

Recommendations and Reasons

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Lenalidomide for multiple myeloma

Product: lenalidomide (Revlimid®)

Class of Drugs: immunomodulatory agent

Reason for Use: newly-diagnosed multiple myeloma after stem-cell transplantation

Manufacturer: Celgene Inc.

Date of Review: November 13, 2013

CED Recommendation

The CED recommended lenalidomide (Revlimid®) not be funded for the maintenance treatment of newly-diagnosed multiple myeloma after stem-cell transplantation. Studies showed that this treatment improves progression-free survival and time to tumour progression. The CED noted that although the improvement in progression-free survival was clinically meaningful, the treatment was not cost-effective.

Executive Officer Decision*

Based on the CED's recommendation and an agreement with the manufacturer to help address concerns raised by the CED, the Executive Officer decided to fund lenalidomide (Revlimid®) through the Ontario Drug Benefit's (ODB) Exceptional Access Program for the maintenance treatment of newly-diagnosed multiple myeloma after stem-cell transplantation according to specific criteria.

Funding Status*

Funded through the ODB's Exceptional Access Program (EAP) according to specific criteria.

(EAP criteria can be found at: http://www.health.gov.on.ca/en/pro/programs/drugs/eap_criteria.aspx)

** This information is current as of the posting date of the document. For the most up-to-date information on Executive Officer decision and funding status, see: www.health.gov.on.ca/en/pro/programs/drugs/status_single_source_subm.aspx.*

Highlights of Recommendation:

- Two studies, IFM 2005-02 and CALGB 100104, showed that lenalidomide improved disease control as measured by progression-free survival and time to tumour progression when used as maintenance therapy in patients with newly-diagnosed multiple myeloma following treatment with stem-cell transplant. The CALGB 100104 study demonstrated that lenalidomide improved overall survival, while the IFM 2005-02 study showed no difference in overall survival.
- Quality of life was not measured in either study.
- In both studies, lenalidomide was associated with increased side effects, including hematological effects and the development of secondary cancers.
- The average cost per 28-day cycle of lenalidomide is approximately \$10,000. Based on economic analyses conducted by the manufacturer and by the pan-Canadian Oncology Drug Review, lenalidomide was not considered cost-effective.

Background:

Multiple myeloma, also known as myeloma, is a cancer of the bone marrow. Multiple myeloma is incurable in the majority of cases. The five and ten year survival rates for all patients are approximately 35% and 17%, respectively. For patients younger than 60 years of age, the ten year survival rate is 30%.

Some patients with multiple myeloma are diagnosed while not showing symptoms of the disease. These patients are generally not treated immediately. Patients showing symptoms of myeloma are treated primarily with anti-myeloma drug therapy and autologous hematopoietic stem cell transplantation (ASCT). Strategies to increase the efficacy of these treatments have been explored.

Detailed Discussions:

- For this evaluation, the CED took into consideration:
 - Findings from the pan-Canadian Oncology Drug Review (pCODR) and the recommendation of the pCODR Expert Review Committee (PERC);
 - Feedback from Cancer Care Ontario's (CCO) Hematology Disease Site Group (DSG);
 - Information in the manufacturer's submission;
 - One patient group submission.
- The CED evaluated two randomized, double-blind, placebo-controlled, phase III trials, IFM 2005-02 and CALGB 100104, that assessed the efficacy and safety of lenalidomide maintenance therapy compared to placebo maintenance in patients with newly-diagnosed multiple myeloma following treatment with autologous stem cell transplant (ASCT).
- In both studies, lenalidomide demonstrated a statistically and clinically significant improvement in disease control as measured by progression free survival (PFS) and time to tumour progression (TTP). The improvement in PFS was considered clinically meaningful,

as considerable morbidity can occur in multiple myeloma patients who experience progression.

- Lenalidomide demonstrated a statistically significant advantage in overall survival (OS) compared with placebo in the CALGB 100104 study, but the IFM 2005-02 study did not show a difference in overall survival. The CED questioned the difference in OS results between the two studies but noted it is increasingly difficult to demonstrate an OS advantage in multiple myeloma due, in large part, to the number of treatment options that can be applied after initial therapy.
- Quality of life (QOL) was not measured in either study. The CED had concerns about the lack of QOL data, as the expectation is that QOL will improve or be maintained when using a treatment for an extended period of time, such as in this clinical setting. The effect of lenalidomide maintenance therapy on QOL is uncertain.
- The use of lenalidomide in the maintenance setting was associated with increased adverse effects, especially with respect to hematological toxicities. Lenalidomide was also associated with increased risk of secondary malignancies. The CED questioned whether the potential benefits of lenalidomide, such as improvements in PFS and OS, could be offset by the potential added risks. Furthermore, the increased risk of second primary malignancies and other serious toxicities may require additional monitoring and health care resources.
- At the recommended dose of 10 - 15 mg per day, the average cost per 28-day cycle of lenalidomide is \$10,108 - \$10,696. Based on economic analyses conducted by the manufacturer and pCODR, lenalidomide was not considered cost-effective.
- Ontario received one patient group submission that was considered during the CED's deliberations. The patient submission highlighted the impact of the disease and patients' wishes for treatments that have decreased side effects, improve QOL, and lead to better disease control and extension of life. Some patients may be willing to accept the risk of secondary malignancies and other side effects if their survival may be extended.
- Overall, there are two clinical trials demonstrating statistically significant improvements in PFS and TTP with the use of lenalidomide in the maintenance setting. Although OS improved in the CALGB 100104 study, there was no OS advantage demonstrated in the IFM 2005-02 study. In addition, it is unknown whether QOL is improved with lenalidomide. Finally, lenalidomide was not considered cost-effective.

Committee to Evaluate Drugs (CED)

The Committee to Evaluate Drugs (CED) is comprised of practicing physicians, pharmacists, health economists, and patient representatives. In conducting its review, the CED considers data contained in the drug manufacturer's submission, input provided by patient groups, findings from the national Common Drug Review and the pan-Canadian Oncology Drug Review, and other scientific information as necessary.

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