

## Recommendations and Reasons

### Committee to Evaluate Drugs (CED)

## Everolimus

**Product:**

EVEROLIMUS (Afinitor®)

**Class of drugs:**

anti-cancer agent; mTOR inhibitor

**Indication:**

metastatic renal cell carcinoma

**Manufacturer:**

Novartis Pharmaceuticals Canada Inc.

### CED Recommendation

The CED recommended that everolimus (Afinitor®) not be funded. The CED acknowledged that everolimus has been shown to reduce the risk of disease progression in patients with metastatic renal cell carcinoma whose disease has progressed on alternative therapies, but noted that this drug does not provide value for money at the submitted price.

### Executive Officer Decision

Based on the CED's recommendation and an agreement with the manufacturer that addresses cost, the Executive Officer decided to fund everolimus (Afinitor®) through the Exceptional Access Program according to specific criteria.

### Status

Funded through the Exceptional Access Program.

### Highlights of Recommendation:

- ◆ Everolimus is an oral anti-cancer drug indicated for the treatment of metastatic renal cell carcinoma (kidney cancer that has spread to other parts of the body).
- ◆ The Committee reviewed a single clinical study evaluating the efficacy of everolimus in patients with metastatic renal cell carcinoma whose disease had progressed on sunitinib, sorafenib, or both of these treatments. The study found that relative to placebo, everolimus prolonged progression-free survival (the length of time that a patient's disease remains stable and does not worsen). When the study was stopped, the median progression-free survival time was 4.0 months in patients who were treated with everolimus and 1.9 months in patients who received placebo, representing a 70% relative reduction in the risk of disease progression.
- ◆ Everolimus costs \$186 per day. Based on the CED's assessment, this drug does not provide value for money at the submitted price.
- ◆ **Overall, the Committee acknowledged that everolimus has been shown to reduce the risk of disease progression in patients with metastatic renal cell carcinoma whose disease has progressed on alternative therapies, but noted that this drug is not cost-effective.**

### Background:

Metastatic renal cell carcinoma refers to kidney cancer that has spread to other parts of the body (e.g. to the lungs, lymph nodes, brain and liver).

For patients with metastatic renal cell carcinoma, cure is usually not possible and treatment is directed at controlling symptoms and prolonging survival. Treatments used in supportive care to control symptoms may include pain medications, bisphosphonates and radiotherapy for bone metastases, colony stimulating factors for neutropenia, medication to improve appetite, and nutritional support. Anti-cancer drug treatments consist of immunotherapy (interferon-alpha, interleukin-2), multi-kinase inhibitors (sunitinib, sorafenib), and mTOR inhibitors (temsirolimus, everolimus).

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## Detailed Discussion:

- ♦ A randomized controlled study (Motzer et al. Lancet 2008) enrolled 410 patients with metastatic renal cell carcinoma whose disease had progressed on sunitinib, sorafenib, or both of these drugs. Patients were randomly assigned in a two to one ratio to receive everolimus or placebo in conjunction with best supportive care. On disease progression, patients initially randomized to placebo were allowed to cross-over to receive everolimus. The study was designed to end after 290 progression events; however, the results of the second interim analysis showed a significant difference in efficacy between the study groups, and the trial was halted after 191 progression events.
- ♦ At the second interim analysis, the median progression-free survival time was 4.0 months in the everolimus group and 1.9 months in the placebo group. In the 60-day efficacy update, the median progression-free survival was 4.9 months with everolimus and 1.9 months with placebo.
- ♦ The study reported no significant difference in overall survival time between patients on everolimus and those on placebo. However, the overall survival results might have been confounded by the high rate of patient cross-over from placebo to everolimus treatment.
- ♦ The Committee noted that although there is no direct evidence of improved overall survival with everolimus, this treatment has been shown to prolong progression-free survival. There is increasing evidence that progression-free survival is correlated to overall survival in the metastatic renal cell carcinoma setting.
- ♦ As part of this review, the Committee took into consideration a submission provided by a patient group. The Committee agreed that patients with metastatic renal cell carcinoma whose disease has progressed on multi-kinase inhibitors currently have no proven therapeutic options and that additional treatments are needed in this setting.
- ♦ Everolimus costs \$186 per day. Based on the CED's assessment, everolimus does not represent value for money at the submitted price.
- ♦ **Overall, the CED acknowledged the clinical benefits of everolimus and the therapeutic need for this treatment, but was concerned with the high drug cost.**

*The CED worked jointly with a subcommittee involving cancer experts to review this cancer drug, as is done for all other cancer drug treatments.*

## EAP Funding:

Based on the CED's recommendation and an agreement with the manufacturer that addresses cost, the Executive Officer decided to fund everolimus (Afinitor®) through the Exceptional Access Program according to specific criteria.

The EAP criteria can be found at: [http://www.health.gov.on.ca/english/providers/program/drugs/eap\\_criteria.html](http://www.health.gov.on.ca/english/providers/program/drugs/eap_criteria.html)



Ministry of  
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