

## **Record of Recommendation**

### **Re: Funding Everolimus (Afinitor<sup>®</sup>) for the treatment of Metastatic Renal Cell Carcinoma**

**April 27, 2010**

Discussion facilitated using the Decision Making Framework.

- All present will vote electronically when the vote is called by the Chair. The voting process will be completed by 5 pm on May 10, 2010. The decision will be made by a majority with dissenting voters given the opportunity to record their opinion. Dissenting opinions must be recorded within seven days of the result of the vote being announced.
- Core values and principles were reviewed and discussed along with competing obligations, constraints and relevant information.
- Options for a recommendation to the Deputy Minister were reviewed and each option was discussed. Two options were identified at this time:
  - 1) Approval of funding with restrictions
  - 2) Denial of funding
- An analysis of the projected benefits and burdens of each option was discussed.

#### **Background:**

- ✓ There are several targeted therapies used in the treatment of metastatic renal cell carcinoma. Sunitinib and sorafenib target the vascular endothelial growth factor pathway. Temsirolimus and everolimus target the mTOR pathway.
- ✓ Temsirolimus is an IV therapy while everolimus is an oral therapy.
- ✓ Current first line treatments in metastatic renal cell carcinoma are oral sunitinib (for clear cell, PS 0-1) or IV temsirolimus (any pathology, poor risk disease). Sunitinib is usually used as the first line agent.
- ✓ Sorafenib can be used as a second line therapy after failure of interferon.

#### Projected Benefits:

- ✓ In a Phase III double blind, placebo controlled trial, everolimus was studied in patients who had progressed on sunitinib/sorafenib or both. Patients may also have had bevacizumab, interferon or interleukin 2. The primary endpoint was progression free survival (PFS). Patients had been heavily pretreated in both the treatment and placebo groups. Once patients progressed they were able to get active drug if they were on placebo (cross-over).
- ✓ Results showed an increase in PFS at the first analysis from 1.9 months with the placebo group to 4.0 months in the everolimus group, and from 1.87 months to 4.9 months at the second analysis. Everolimus was associated with a decrease in risk of progression and increase in stability rate. Median overall survival was not statistically significant between the two groups, which may have been influenced by cross-over to active treatment in the placebo group.

#### Projected Burdens:

- ✓ The most common grade 1 or 2 adverse effects were stomatitis, rash, fatigue, asthenia, and diarrhea. Patients receiving everolimus had higher rates of grade 3 or 4 stomatitis, infections and non-infectious pneumonitis.
- ✓ The approximate cost per patient per month is \$5,407.50. The predicted budget impact in 2010/11 is \$162,225 (6 patients), in Year 2 is \$189,263 (7 patients) and in Year 3 is \$216,300 (8 patients).
- ✓ Estimated cost per life year gained and cost per quality adjusted life year is estimated to be \$ \$73,434 and \$99,696 respectively.

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#### Result of Vote:

The vote was conducted electronically. The question the Committee was asked to vote on is:

“Should the Committee support a recommendation to the Deputy Minister of Health to fund everolimus as a single agent for metastatic renal cell carcinoma with documented clear cell histology who have a Karnofsky performance status of 70% or higher after progression or intolerance to the multi-targeted tyrosine kinase inhibitors (TKIs), sunitinib, and/or sorafenib”

- **The result of the vote was a majority in favor of not recommending funding.**
- **The Deputy Minister of Health has accepted this recommendation.**