

Sunitinib (for Metastatic Renal Cell Carcinoma)

Product:

SUNITINIB (Sutent®) 12.5mg, 25mg, 50mg capsule

Class of drugs:

Multi-kinase inhibitor; anti-cancer agent

Indication:

Treatment of metastatic renal cell carcinoma (MRCC) or kidney cancer

Manufacturer:

Pfizer Canada Inc.

CED Recommendation

The CED recommended that sunitinib (Sutent) be funded through the Exceptional Access Program (EAP) for the first-line treatment of metastatic renal cell carcinoma (MRCC) if the price is reduced. The CED's recommendation was made on the basis that the drug appears to be more effective and better tolerated than interferon-alpha for treating this disease, but is significantly more expensive.

Executive Officer Decision

Taking into consideration the CED's review and recommendation and based on a subsequent pricing agreement, the Executive Officer decided to fund sunitinib (Sutent) as first-line and second-line treatment for MRCC through the Exceptional Access Program, according to specific criteria.

Status

Funding available through the Ontario Public Drug Programs via the Exceptional Access Program.

Highlights of Recommendation:

- ◆ Sunitinib (Sutent) is a new drug treatment for patients with Metastatic Renal Cell Carcinoma (MRCC). MRCC is kidney cancer that has spread to other parts of the body.
- ◆ The Committee initially considered sunitinib (Sutent) in the second-line treatment of MRCC (i.e., in patients who have failed or cannot tolerate first-line therapy). The clinical and economic evidence for sunitinib (Sutent) for second-line therapy was not compelling.
- ◆ The Committee subsequently considered the use of sunitinib (Sutent) in first-line treatment.
- ◆ An interim analysis of a large trial comparing sunitinib (Sutent) and interferon-alpha (the current first-line therapy) supports using sunitinib (Sutent) as first-line treatment for MRCC. Sunitinib (Sutent) was shown to improve the length of time patients were surviving without disease progression.
- ◆ Sunitinib (Sutent) was also better tolerated than interferon-alpha.
- ◆ However, the high cost of sunitinib (Sutent) renders the therapy much less cost-effective when compared to interferon-alpha for the treatment of MRCC.
- ◆ Interferon-alpha is currently reimbursed through the Exceptional Access Program (EAP) for the treatment of MRCC.
- ◆ The Committee indicated it is highly likely that sunitinib (Sutent) would replace interferon-alpha for treating MRCC if it is funded.

- ◆ Overall, the Committee noted that **first-line therapy with sunitinib (Sutent) appears to be more effective and better tolerated than interferon-alpha. However, sunitinib (Sutent) therapy is not considered cost-effective when compared to interferon-alpha for the treatment of MRCC.**
- ◆ Therefore, the Committee recommended that sunitinib (Sutent) be funded through the EAP for first-line treatment of MRCC, if the price is reduced.

Background:

Metastatic renal cell carcinoma is a form of kidney cancer that has spread beyond the kidney.

Renal cell cancer can spread to the lungs, lymph nodes, brain and liver. In about 30 percent of patients, the cancer has spread or metastasized by the time of diagnosis. After aggressive surgery, the first-line, or standard treatment for MRCC has been with drugs that stimulate the immune system, such as interferon-alpha or interleukin-2. However, these drugs are not suitable for all patients; and interferon-alpha appears to be of less benefit than some newer anti-cancer drugs.

Sunitinib (Sutent) is a new alternative for patients with MRCC. The drug works by targeting specific enzymes involved in the growth and survival of cancer cells. By disrupting this signalling, sunitinib (Sutent) prevents renal carcinoma cells from forming new blood vessels that sustain the growth of a cancerous tumour.

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Detailed Discussion:

- ◆ In March 2007, the Committee considered sunitinib (Sutent) for second-line therapy of MRCC. At that time, the Committee felt there were no compelling data from published randomized phase III trials to support this indication. The Committee was also concerned about the lack of pharmacoeconomic data to support the drug's cost-effectiveness for second-line treatment.
- ◆ In June 2007, the Committee considered the funding of sunitinib (Sutent) for the first-line treatment of MRCC.
- ◆ The Committee reviewed studies evaluating sunitinib (Sutent) for first-line treatment of MRCC, including the associated practice guidelines developed by Cancer Care Ontario's (CCO's) Genitourinary Disease Site Group.
- ◆ The associated practice guidelines state that although immunotherapy has been the standard of care for patients with inoperable locally advanced or metastatic renal cell carcinoma, there is now evidence of important clinical benefit for agents that inhibit angiogenesis in this patient population.
- ◆ The CCO guidelines supporting first-line treatment include a large randomized clinical trial (Motzer et al, *N Engl J Med* 2007 January 11; 356(2):115-124), which reported significantly longer progression-free survival with sunitinib (Sutent) compared with interferon-alpha. At the time of analysis, the duration of progression-free survival was a median of 11 months for patients treated with sunitinib (Sutent), compared with median of five months for patients treated with interferon-alpha; hazard ratio=0.42, [95% confidence interval (CI), 0.32-0.54]; p-value<0.000001.
- ◆ The available data on quality of life from the Motzer et al trial were limited but suggested patient-reported quality of life, as assessed by the Functional Assessment of Cancer Therapy-General (FACT-G), was better with sunitinib (Sutent). Mean total FACT-G scores were higher with sunitinib (Sutent) than interferon-alpha at every assessment time point.

- ◆ The most common side effects associated with sunitinib (Sutent) are fatigue, diarrhea, nausea, hypertension, and suppression of blood counts.
- ◆ The Committee noted that the results of the pharmacoeconomic analysis provided by the manufacturer comparing sunitinib (Sutent) to interferon-alpha for the treatment of MRCC are above the threshold where a therapy is typically considered cost-effective. This is mainly due to the significantly higher price of sunitinib (Sutent) in comparison to interferon alpha (\$6,950 per 6-week cycle versus \$4,500 per 12-week cycle).
- ◆ Overall, the Committee noted that results from a large phase III randomized clinical trial show that sunitinib (Sutent) is more effective and better tolerated when compared to interferon-alpha in the first-line treatment for MRCC. However, using sunitinib (Sutent) for the treatment of MRCC is not considered cost-effective when compared to interferon-alpha therapy. Therefore, the Committee recommended that sunitinib (Sutent) be funded through the EAP (Exceptional Access Program) if the price is reduced.
- ◆ The CED worked jointly with a subcommittee involving cancer experts to review this cancer drug, as is done for all other cancer drug treatments.

Sunitinib (Sutent) is funded through the EAP according to the following criteria:

- ◆ First-line therapy for patients with Memorial Sloan Kettering Prognostic Score of Favourable Risk or an Intermediate Risk; or
- ◆ Second-line therapy for patients where
 - (a) the disease is of clear cell histology; AND
 - (b) they have failed first-line cytokine-based therapy.
- ◆ The prescribed dosage should be 50mg daily for four (4) weeks, followed by two (2) weeks off the Drug Product, in repeated six (6) week cycles.
- ◆ Renewal criteria: Written confirmation from the clinician that the patient has benefited from therapy and is expected to continue to do so.

Cancer Care Ontario (CCO) Information:

Information on CCO chemotherapy regimens for MRCC is available at:

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

CEDAC Recommendation:

(<http://www.cadth.ca/index.php/en/cdr/recommendations>)

The Canadian Expert Drug Advisory Committee (CEDAC) reviewed sunitinib (Sutent) for second-line treatment of MRCC and recommended that it not be listed. CEDAC did not review sunitinib (Sutent) for first-line treatment of MRCC.



Ministry of
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