

CEDAC FINAL RECOMMENDATION on RECONSIDERATION and REASONS for RECOMMENDATION

SUNITINIB MALATE (Sutent™ Resubmission – Pfizer Canada Ltd.)

Description:

Sunitinib is a tyrosine kinase inhibitor that is approved for use in the treatment of gastrointestinal stromal tumour (GIST) and renal cell carcinoma. This recommendation relates solely to the approved indication for the treatment of metastatic renal cell carcinoma of clear cell histology after failure of cytokine-based therapy or in patients who are considered likely to be intolerant of such therapy, which has received a Notice of Compliance with Conditions (NOC/c) from Health Canada.

Dosage Forms:

12.5, 25 and 50 mg tablets. The recommended dose of sunitinib is 50 mg daily, in repeated cycles of four weeks of treatment followed by two weeks without treatment.

Recommendation:

The Canadian Expert Drug Advisory Committee (CEDAC) recommends that sunitinib not be listed for the treatment of metastatic renal cell carcinoma..

Reasons for the Recommendation:

1. There are no data from randomized controlled trials (RCTs) supporting the use of sunitinib in patients who have failed cytokine-based therapy, the group of patients reflected by the approved indication for sunitinib and included in the economic evaluation submitted by the manufacturer.
2. Sunitinib costs \$6,950 for a six week cycle of therapy. The economic evaluation submitted by the manufacturer reported an incremental cost-effectiveness of sunitinib of \$42,000 per life year gained and \$56,000 per quality adjusted life year (QALY) in comparison to palliative supportive care in patients who had failed cytokine-based therapy. The treatment effect was based on an uncontrolled trial of sunitinib while disease progression was based on information from a database. The model predicted a survival advantage of 1.0 years and an improved quality of life, neither of which can be confirmed due to the lack of controlled studies in this patient group, making the true cost-effectiveness of sunitinib uncertain. Therefore, the Committee felt that the survival benefit and cost-effectiveness of sunitinib had not been established in patients who have failed cytokine-based therapy.

Common Drug Review

Summary of Committee Considerations:

The Committee considered the results of a systematic review of RCTs in patients with metastatic renal cell carcinoma. One RCT in treatment naïve patients met the inclusion criteria for the systematic review. The RCT compared sunitinib with interferon alpha in 750 patients who had not received prior systemic therapy for renal cell carcinoma. The primary outcome for the study was progression-free survival (PFS). After a planned interim analysis, patients in the interferon alpha group who developed progressive disease were allowed to cross over to sunitinib therapy. The Committee considered the results from this interim analysis which showed that sunitinib was associated with a statistically significant increase in PFS compared to interferon alpha (47 vs 22 weeks). At the time of the interim analysis, median overall survival had not been reached. Although there was a trend towards an improved hazard ratio for overall survival with sunitinib, this difference did not meet the pre-specified level of statistical significance. Sunitinib therapy was also associated with a statistically significant partial response rate compared to placebo (31% vs. 6%) although no patient in either group experienced a complete response.

The Committee also considered the results of two uncontrolled trials of sunitinib in patients who had failed cytokine-based therapy.

The incidence of patients experiencing at least one serious adverse event was higher in patients receiving sunitinib (31%) than interferon alpha (22%), although interpretation of these rates is complicated by differences in the median duration of treatment with sunitinib (169 days) vs interferon alpha (123 days). More patients in the sunitinib group experienced diarrhea, vomiting, hypertension and hand-foot syndrome while more patients in the interferon group experienced fatigue.

Of Note:

1. Both published and unpublished data were reviewed and taken into consideration in making this recommendation.

Background:

CEDAC provides formulary listing recommendations to publicly funded drug plans. Recommendations are based on an evidence-based review of the medication's effectiveness and safety and an assessment of its cost-effectiveness in comparison to other available treatment options. For example, if a new medication is more expensive than other treatments, the Committee considers whether any advantages of the new medication justify the higher price. If the recommendation is not to list a drug, the Committee has concerns regarding the benefit/harm of the medication, and/or concerns about whether the medication provides good value for public drug plans.

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