

## Sorafenib (for hepatocellular carcinoma)

### Product:

SORAFENIB (Nexavar®) 200mg tablet

### Class of drugs:

Multi-kinase inhibitor; anti-cancer agent

### Indication:

Treatment of hepatocellular carcinoma (HCC)

### Manufacturer:

Bayer Inc.

## CED Recommendation

The CED recommended that sorafenib (Nexavar) be funded through the Exceptional Access Program for the treatment of advanced hepatocellular carcinoma (HCC) according to specific criteria. The CED acknowledged that sorafenib (Nexavar) has been shown to provide a survival advantage in certain patients with HCC but noted that it is not cost-effective.

## Executive Officer Decision

Based on the CED's recommendation and a subsequent pricing agreement with the manufacturer, the Executive Officer decided to fund sorafenib (Nexavar) through the Exceptional Access Program for the treatment of HCC, according to specific criteria.

## Status

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

### Highlights of Recommendation:

- ◆ Sorafenib (Nexavar) is an oral drug indicated for the treatment of hepatocellular carcinoma (liver cancer) and metastatic renal cell carcinoma (kidney cancer). This particular review considered the funding of sorafenib (Nexavar) for the treatment of advanced hepatocellular carcinoma (HCC).
- ◆ The Committee reviewed two studies that compared sorafenib (Nexavar) to placebo in patients with advanced HCC. The patients enrolled in the two studies had liver disease that was classified as Child-Pugh Class A, indicating that these patients still maintained adequate liver function. The studies found that sorafenib (Nexavar) provided a small (2.8 months) survival advantage compared with placebo.
- ◆ There is no evidence that sorafenib (Nexavar) is effective in patients with more severe liver disease (i.e. patients whose disease is Child-Pugh Class B or C).
- ◆ Sorafenib (Nexavar) costs \$175 per day. An economic evaluation found that sorafenib (Nexavar) is not cost-effective.
- ◆ **Overall, the Committee noted that sorafenib (Nexavar) has been shown to improve survival in patients with advanced HCC whose liver disease is of no worse severity than Child-Pugh Class A. The Committee also recognized that there are limited effective treatment options for advanced HCC. However, sorafenib (Nexavar) is not cost-effective at the submitted price. In light of the above, the Committee recommended that funding for this treatment be considered through the Exceptional Access Program (EAP).**

### Background:

Hepatocellular carcinoma (HCC) is the most common form of liver cancer. HCC usually occurs as a result of chronic hepatitis or cirrhosis of the liver.

Treatments for HCC can be divided into those delivered with the intention to cure and those that are palliative (i.e. treatments that ease symptoms and/or to delay disease progression). Surgery and transplantation have the potential to cure the disease, but they are generally offered to only 30-40% of patients at early stages of the disease. There is no accepted standard treatment for advanced HCC. Palliative therapies include radiofrequency ablation, transarterial chemoembolization, and chemotherapy. None of these treatments have been shown to improve survival.

The Child-Pugh classification system is used to assess the severity of a patient's liver disease, the prognosis, and the appropriate treatment. A Child-Pugh score of 5-6 is considered class A (well-compensated disease); 7-9 is class B (significant functional compromise); and 10-15 is class C (decompensated disease).

Sorafenib (Nexavar) is a new oral drug indicated for advanced HCC in patients with unresectable liver cancer.

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## Detailed Discussion:

- ◆ The Committee considered the funding of sorafenib (Nexavar) for the treatment of advanced HCC on two occasions, initially in April 2008 and again in July 2008.
- ◆ The focus of the Committee's review was the SHARP study (*New England Journal of Medicine* 2008;359:378-90). This is a randomized controlled trial that compared sorafenib (Nexavar) to placebo in patients with advanced HCC who had Child-Pugh Class A disease. The study found that median survival and time-to-disease-progression were nearly 3 months longer for patients treated with sorafenib (Nexavar) than for patients who took placebo. The median overall survival was 10.7 months in the sorafenib (Nexavar) treated group and 7.9 months in the placebo group.
- ◆ A second study, the Asia-Pacific Trial (not yet published, currently available in abstract only), reported results that were similar to those observed in the SHARP study.
- ◆ There are no studies on the efficacy of sorafenib (Nexavar) in patients with advanced HCC who have Child-Pugh Class B or C disease. The Committee indicated that without direct evidence of efficacy and safety in this patient population, the routine use of sorafenib (Nexavar) in patients with Child-Pugh B and C disease could not be recommended.
- ◆ Common side effects with sorafenib (Nexavar) include high blood pressure, bleeding, rash, hand-foot reactions (redness, pain, swelling on the hands and feet), diarrhea and fatigue.
- ◆ Sorafenib (Nexavar) costs \$175 per day. An economic evaluation found that the cost is extremely high relative to the degree of benefit provided by the treatment and that sorafenib (Nexavar) is not cost-effective.
- ◆ Overall, the Committee noted that sorafenib (Nexavar) has been shown to improve survival in patients with advanced HCC whose liver disease is of no worse severity than Child-Pugh Class A. The Committee also recognized that there are limited effective treatment options for advanced HCC. However, sorafenib (Nexavar) is not cost-effective at the submitted price. In light of the above, the Committee recommended that funding for this treatment be considered through the Exceptional Access Program (EAP).

## EAP Criteria:

- ◆ The CED recommended that sorafenib (Nexavar) be funded through the Exceptional Access Program (EAP) according to the following criteria:
  - For patients with Child-Pugh Class A advanced hepatocellular carcinoma; and
  - The patient's ECOG status is 0, 1, or 2; and
  - The patient has either progressed on trans-arterial chemoembolization (TACE) or is not suitable for the TACE procedure.
  - Renewal criteria: No progression of the patient's disease, as documented on radiography and/or scan results.
  - Not reimbursed if used with induction or adjuvant intent along with other curative-intent treatments.
  - Not reimbursed if used for maintenance therapy after trans-arterial chemoembolization.
  - Not reimbursed if the patient has Child-Pugh B or Child-Pugh C cirrhosis.
- ◆ The CED worked jointly with a subcommittee involving cancer experts to review this cancer drug, as is done for all other cancer drug treatments.

## Cancer Care Ontario Information:

Information about CCO chemotherapy regimens for HCC is available at: [http://www.cancercare.on.ca/index\\_chemoRegimensbyDisease.htm](http://www.cancercare.on.ca/index_chemoRegimensbyDisease.htm)



Ministry of  
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