

Record of Recommendation

Re: Funding sorafenib (Nexavar®) in Advanced Hepatocellular Carcinoma (HCC)

November 12, 2008

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 December 2, 2008. 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:

- ✓ Hepatocellular Carcinoma (HCC) is the most common primary liver malignancy, the sixth most common cancer worldwide and the third most common cause of cancer-related death.
- ✓ Patients affected by HCC usually have two diseases, a primary liver tumor and cirrhosis of the liver (70-90% of cases).
- ✓ Treatment for early stage HCC can include resection and transplantation.
- ✓ For advanced HCC, transarterial embolization/chemoembolization is widely used. This only benefits patients with preserved liver function and asymptomatic multimodal tumours (about 30% of patients).

Projected Benefits: in the treatment of advanced hepatocellular carcinoma:

- ✓ Versus placebo, use of sorafenib in patients with advanced HCC leads to an increase in overall survival (10.7 months versus 7.9 months) and an increase in median time to progression (5.5 months versus 2.8 months). This is the first systemic therapy to show significant benefit in advanced HCC.
- ✓ There was no significant effect on time to symptomatic progression and conclusions regarding effects on quality of life cannot be made.
- ✓ For patients with HCC who are not candidates for curative or other palliative modalities such as transarterial embolization, sorafenib may provide the only therapeutic option.

Projected Burdens:

- ✓ The most frequently reported grade 3 or 4 serious adverse events in the sorafenib versus placebo arms were diarrhea (8 vs 2%; $p < 0.001$) hand foot skin reactions (8 vs $< 1\%$; $p < 0.001$), hypertension (2% vs 1%; $p = 0.17$), and abdominal pain (2% vs 1%; $p = 0.17$).
- ✓ Sorafenib treatment (400mg twice daily) costs \$5250.00 per month. The median length of therapy in the study (time to radiological progression) was 5.5 months which translates to an average cost of \$28,875 per treated patient.
- ✓ This policy recommendation would require incremental funding within the Province of Nova Scotia of approximately \$288,750 (for 10 patients per year).

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 to fund sorafenib (Nexavar®) as a single agent first line systemic therapy option in adult patients with a diagnosis of hepatocellular carcinoma (HCC) who are not candidates for curative intent treatments (transplantation, hepatic resection), or other well established palliative interventions (ablation, transcatheter arterial chemo-embolization (TACE), internal radiation).

Candidates for sorafenib (Nexavar®) are patients affected by HCC with Child-Pugh Class A liver dysfunction (mild hepatic impairment) and ECOG performance status 0-1. This patient population may have either progression of disease or are not suitable candidates for curative interventions (hepatic resection) or other palliative therapies (ablation, TACE, internal radiation).

Since sorafenib (Nexavar®) is an oral drug, funding would be through the Nova Scotia Pharmacare Programs.

- **The result of the vote was a majority in favor of recommending funding. There were no dissenting opinions recorded.**