pan-Canadian Oncology Drug Review
Final Economic Guidance Report

Pazopanib (Votrient) Resubmission for Metastatic Renal Cell Carcinoma

August 29, 2013
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INQUIRIES

Inquiries and correspondence about the pan-Canadian Oncology Drug Review (pCODR) should be directed to:

pan-Canadian Oncology Drug Review
1 University Avenue, suite 300
Toronto, ON
M5J 2P1

Telephone:  416-673-8381
Fax:   416-915-9224
Email:   info@pcodr.ca
Website:  www.pcodr.ca
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1 ECONOMIC GUIDANCE IN BRIEF

1.1 Background

The main economic analysis submitted to pCODR by GlaxoSmithKline (GSK), compared pazopanib to sunitinib for patients with metastatic renal cell carcinoma (mRCC). This patient population reflects patients from the COMPARZ trial. Pazopanib is administered orally. The COMPARZ trial was a randomized, active-controlled, non-inferiority Phase III study in patients with mRCC who had not received prior systematic chemotherapy. Current standard of care in Canada for first-line mRCC is sunitinib.

According to the pCODR Clinical Guidance Panel (CGP), the comparison of pazopanib to sunitinib in this indication was considered appropriate.

Patient advocacy groups considered the following factors important in the review of pazopanib, which are relevant to the economic analysis: improvement in a patient’s quality of life and survival and an accessible treatment that will enable them to continue to work and maintain a normal family life. A full summary of the patient advocacy group input is provided in the pCODR Clinical Guidance Report.

- The submitted economic analysis explicitly considered improvements in quality of life by applying utility scores and measuring outcomes in quality-adjusted life years. The quality of life information was collected from the PISCES trial.

- The model has not considered whether pazopanib will enable patients to spend more time working or with family - the model adopts the perspective of the publicly funded health care system which is appropriate for pCODR because drug funding recommendations must be considered from a health system perspective.

The Provincial Advisory Group (PAG) considered that the following factors would be important to consider if implementing a funding recommendation for pazopanib, and which are relevant to the economic analysis: differences between pazopanib and sunitinib with respect to costs, treatment outcomes, side effect profile, and information on the sequential use of pazopanib. Oral dosing and administration, patient compliance, and use of pazopanib as adjuvant treatment of mRCC would also be appropriate to consider. A full summary of Provincial Advisory Group input is provided in the pCODR Clinical Guidance Report.

- Oral administration of pazopanib was not explicitly considered in the submitted model as pazopanib compared with sunitinib, also an oral treatment.

- Evidence to support use of pazopanib as adjuvant treatment is lacking. This was not explicitly considered in the submitted model.

At the list price, pazopanib costs $37 per 200 mg tablet. At the recommended dose of 800 mg per day, the average cost per day in a 28-day course of pazopanib is $148 and the average cost per 28-day course is $4,144.

At the list price, sunitinib costs $62, $124 or $248 per 12.5mg, 25mg and 50mg capsule, respectively. At the recommended dose of 50 mg per day, the average cost per day in a 42-day course of sunitinib is $165 and the average cost per 28-day course is $4,632.
1.2 Summary of Results

The Economic Guidance Panel’s best estimate of the incremental cost-effectiveness of pazopanib is that it’s cost-saving (between $7,215 and $7,316 per patient) when compared to sunitinib (at the current price) in patients with 1st line mRCC. This estimate is based on reanalyses conducted by the Economic Guidance Panel using the submitted price and the model submitted by GSK.

The Economic Guidance Panel’s estimate differed from the submitted estimates. This is primarily because the EGP reanalyses assumed equal efficacy and impact on quality of life (i.e. utilities) for pazopanib and sunitinib based on the COMPARZ and PISCES trials and the CGP interpretation of COMPARZ as representing similar efficacy of pazopanib and sunitinib.

The EGP’s best estimate is also based on currently available evidence on the impact of pazopanib on progression-free survival and quality of life, as well as the current price of its comparator, sunitinib. However, should the unit price of sunitinib be reduced, the ability of pazopanib to be cost-saving can be substantially diminished unless the price of pazopanib is also reduced.

According to the economic analysis that was submitted by the manufacturer, when pazopanib was compared to placebo using a partition-survival analysis over a 37.5-month (3.13 years) time horizon:
- Pazopanib is expected to result in cost savings of $6,986 per patient. Incremental costs for pazopanib are based on a model where survival and progression are modelled independently. This allows for a patient’s risk of dying to be a function of time and not only influenced directly by the increasing proportion of patients in the post-progression state, which the CGP considered as inappropriate. The model included drug treatment medication cost, administration costs, dispensing costs, and other costs associated with pazopanib and sunitinib treatments (e.g. costs of hospitalizations, specialist’s visits, etc.), cost of routine care and follow-up, and cost of post-treatment anti-cancer therapy for pazopanib and sunitinib. Utilization data was obtained from patients in COMPARZ study.
- The extra clinical effect (ΔE) of pazopanib is 0.089 QALYs (2.7 weeks). A significant part of this gain is from over-estimating PFS gain, which arises when survival and progression are modelled independently in the partition-survival methodology, which the CGP considered as inappropriate. Clinical effects are based on overall survival and investigator-assessed PFS in the ITT population of the COMPARZ study. Utility values are based on EQ-5D assessments from the PISCES trial.

Therefore, the Submitter estimated that pazopanib is dominating sunitinib (i.e. more effective at a lower cost) as a 1st line treatment for patients with mRCC.
1.3 Summary of Economic Guidance Panel Evaluation

If the EGP estimates of ΔC, ΔE and the ICER differ from the Submitter’s, what are the key reasons?

The manufacturer submitted an economic evaluation using efficacy and utility values from COMPARZ and PISCES trials respectively. Evidence from the trials indicates that pazopanib appears to have similar efficacy and impact on quality of life as sunitinib. Also, the manufacturer had reported differences in progression-free survival (PFS) from COMPARZ trial depending on assessment method; investigator-assessed, showing PFS favorable to pazopanib, versus independent review committee (IRC-assessed) showing favorable PFS for sunitinib. The Clinical Guidance Panel determined that based on submitted evidence, pazopanib and sunitinib appear to have similar efficacy and impact on quality of life.

Were factors that are important to patients adequately addressed in the submitted economic analysis?

Yes. Based on patient advocacy group input, patients considered the following factors important in the review of pazopanib and which were relevant to the economic analysis: improvement in a patient’s quality of life and enabling them to spend more family time. These factors were addressed in the economic analysis when possible and appropriate.

Is the design and structure of the submitted economic model adequate for summarizing the evidence and answering the relevant question?

The manufacturer submitted a partitioned-survival based analysis in which patients transitioned between three health states; alive and progression-free, disease progression and death. Transition rates between these health states were determined by progression-free survival and overall survival estimates from COMPARZ study. However, by using the partitioned-survival analysis approach, survival and progression are modelled independently and this allows a patient’s risk of dying to be a function of time and not influenced directly by the increasing proportion of patients in the post-progression state. However, this limitation was irrelevant to the results of pazopanib in this review based on the submitted evidence.

For key variables in the economic model, what assumptions were made by the Submitter in their analysis that had an important effect on the results?

In the submitted base-case analysis, the manufacturer used the investigator-assessed PFS which was favorable to pazopanib as well utility values that showed pazopanib to have a better impact on quality of life than sunitinib. Based on CGP interpretation of submitted evidence, it was determined that pazopanib and sunitinib appear similar in terms of efficacy and quality of life.

Were the estimates of clinical effect and costs that were used in the submitted economic model similar to the ones that the EGP would have chosen and were they adequate for answering the relevant question?

Yes - this is a well designed study with mostly appropriate estimates in the submitted analysis.

1.4 Summary of Budget Impact Analysis Assessment

What factors most strongly influence the budget impact analysis estimates?

The manufacturer submitted a budget impact analysis that was not specific to any Canadian public drug plan. The analysis estimates the decreased costs for the three years...
subsequent to the listing of pazopanib for mRCC. The key variables included in the manufacturer’s budget impact analysis are treatment cost and the proportion of these patients who would use pazopanib if available rather than the currently used treatments.

What are the key limitations in the submitted budget impact analysis?
The model structure of the budget impact analysis was appropriate.

1.5 Future Research

What are ways in which the submitted economic evaluation could be improved?
The economic evaluation of pazopanib could have been improved by including long term efficacy and survival data from clinical trials.

Is there economic research that could be conducted in the future that would provide valuable information related to pazopanib in this context?
If pazopanib becomes a standard treatment option for patients with mRCC, an assessment of effectiveness and cost-effectiveness of treatment sequences of pazopanib and other treatments for mRCC would also provide a more accurate reflection of real-world cost-effectiveness and may improve estimates of budget impact.
2 DETAILED TECHNICAL REPORT

This section outlines the technical details of the pCODR Economic Guidance Panel’s evaluation of the economic evidence that is summarized in Section 1. Pursuant to the pCODR Disclosure of Information Guidelines, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations.
3 ABOUT THIS DOCUMENT

This Economic Guidance Report was prepared by the pCODR Economic Guidance Panel and supported by the pCODR Genitourinary Clinical Guidance Panel and the pCODR Methods Team. This document is intended to advise the pCODR Expert Review Committee (pERC) regarding resource implications and the cost-effectiveness of pazopanib for mRCC. A full assessment of the clinical evidence of pazopanib for mRCC is beyond the scope of this report and is addressed by the relevant pCODR Clinical Guidance Report. Details of the pCODR review process can be found on the pCODR website (www.pcodr.ca).

pCODR considers it essential that pERC recommendations be based on information that can be publicly disclosed. Information included in the Economic Guidance Report was handled in accordance with the pCODR Disclosure of Information Guidelines. There was no information redacted from this publicly available Guidance Report.

This Final Economic Guidance Report is publicly posted at the same time that a pERC Final Recommendation is issued. The Final Economic Guidance Report supersedes the Initial Economic Guidance Report. Note that no revisions were made in between posting of the Initial and Final Guidance Reports.

The Economic Guidance Panel is comprised of economists selected from a pool of panel members established by the pCODR Secretariat. The panel members were selected by the pCODR secretariat, as outlined in the pCODR Nomination/Application Information Package and the Economic Guidance Panel Terms of Reference, which are available on the pCODR website (www.pcodr.ca). Final selection of the pool of Economic Guidance Panel members was made by the pERC Chair in consultation with the pCODR Executive Director. The Economic Guidance Panel is editorially independent of the provincial and territorial Ministries of Health and the provincial cancer agencies.
REFERENCES

