PAN-CANADIAN ONCOLOGY DRUG REVIEW

pan-Canadian Oncology Drug Review

Patient Advocacy Group Feedback on a pCODR Expert Review Committee Initial Recommendation

Pazopanib hydrochloride (Votrient) for metastatic renal cell carcinoma

January 5, 2012

Feedback on pERC Initial Recommendation

Name of the drug indication(s):	Pazopanib hydrochloride (Votrient) for metastatic renal cell carcinoma
Name of registered patient advocacy	Kidney Cancer Canada

Comments on the Initial Recommendation

a) Please indicate if the patient advocacy group agrees or disagrees with the initial recommendation:

____ agrees X agrees in part ____ disagree

Please explain why the patient advocacy group agrees, agrees in part or disagrees with the initial recommendation.

Kidney Cancer Canada has two significant concerns with the initial recommendation:

1. **Requirement for patients to prove "unable to tolerate sunitinib".**
   KCC is concerned about how "intolerance to sunitinib" will be determined at the provincial reimbursement level. If intolerance is determined through direct experience with sunitinib, pCODR should clarify, in its recommendations to payers, that the subsequent use of pazopanib is still to be considered a first-line treatment, by clearly distinguishing "intolerance" from "treatment failure/progression". "Intolerance to sunitinib" may in fact occur at different timepoints as many of the intolerable side effects are cumulative with prolonged exposure.
2. **Delays in patient access.**
   KCC is concerned about further delays in patient access while we await head-to-head trials that will resolve perceived uncertainty. For rare cancers such as kidney cancer, such direct comparison trials are rarely conducted – indirect comparisons will often be required. For Votrient, the PISCES and COMPARZ trials are expected to report in June or September 2012, and will require another pCODR submission, another pCODR review period and subsequent provincial reimbursement process deliberations. For patients requiring access to treatment choice in the first line, that choice will potentially be delayed by another full year. Votrient was approved by Health Canada in May 2010 as first-line treatment without conditions of intolerance to sunitinib based upon a global Phase 3 Clinical trial and Level One evidence.

b) Notwithstanding the feedback provided in part a) above, please indicate if the patient advocacy group would support this initial recommendation proceeding to final pERC recommendation ("early conversion"), which would occur within 2(two) business days of the end of the consultation period.

__X__	Support conversion to final recommendation. Recommendation does not require reconsideration by pERC.	____	Do not support conversion to final recommendation. Recommendation should be reconsidered by pERC.

c) Please provide feedback on the initial recommendation. Is the initial recommendation or are the components of the recommendation (e.g., clinical and economic evidence) clearly worded? Is the intent clear? Are the reasons clear?

Pg #	Section Title	Paragraph Line #	Comments and Suggested Changes to Improve Clarity
1	Recommendation	4 Line 5	The words "because there is too much uncertainty, due to the lack of direct comparative trials" are deeply concerning for patients with rare cancers. Given long drug development cycles (often based on a previous standard of care), it is unreasonable to expect to resolve uncertainty with "direct comparative trials". Indeed, the pERC committee noted "pERC recognized that at the time the trial was designed, placebo may have been an appropriate comparator." Indeed, Sutent was not approved when these global studies began. We would prefer to see references in support of indirect comparisons and for pERC to deliberate the risk of accepting such uncertainties. Demanding certainty from head-to-head trials will prevent access to innovative treatments currently in the pipeline for renal cell carcinoma. In the case of Votrient, access to this treatment choice should not be delayed simply because, in this one instance, direct comparison trials are ongoing worldwide. Kidney Cancer Canada believes that, if a drug has been shown to be of clinical benefit, has been acceptably well tolerated (i.e., it has Health Canada approval) and it is economically in line, it should be left to Canadian oncologists and their patients to make the choice between two viable alternatives. Our concern: the Recommendation, as it stands, could potentially add another year of reimbursement deliberations while Canadian patients (outside of BC and Quebec where access is not limited by this condition) await publication of subsequent trials, Re-Submission to pCODR, and subsequent provincial reviews and updates.
2	Summary of pERC Deliberations	Paragraph 4	"pERC also deliberated upon the potential use of pazopanib in patients with disease progression on sunitinib" and "noted that the current standard of care for second-line treatment of advanced or metastatic renal cell carcinoma is everolimus and concluded that there was insufficient reason to support pazopanib use in this setting as everolimus has been studied in patients with metastatic renal cell carcinoma with disease progression on a tyrosine kinase inhibitor." Our concern: The issue, now introduced with "intolerance to sunitinib" as a prior condition for Votrient, is that provincial reimbursement bodies may see a Sutent-tolerability period as the first-line treatment and then deny subsequent access to pazopanib. Patients would then be denied access to a TKI that could offer them significant PFS benefit.

Comments Related to Patient Advocacy Group Input

1	Recommendation	Paragraph 1 Lines 8-13	Barrier to Individual Patient and Physician Choice: The recommendation to prove "intolerance to sunitinib" puts up a barrier to choice for any oncologist and patient who would prefer the safety and side effect profile of Votrient for issues related to manual work or QOL (e.g., to reduce likelihood of hand/foot syndrome and fatigue). Patients with renal cell carcinoma clearly indicated that they need choice in treatment options. Physicians treating kidney cancer will need the greatest latitude to define "intolerance to sunitinib" based upon individual circumstances. Our concern is that prior intolerability to Sutent will be interpreted strictly (and differently) among provincial bodies as we have seen with long-standing and mandatory cytokine prerequisites for Nexavar. In keeping with evidence-based recommendations, we are not aware of any literature, including case reports, that would narrow Votrient use to a specific population of those intolerant to sunitinib.
2	Summary of pERC Deliberations	Paragraph 3 Line 2	On Fatigue as a profound detriment to patient Quality of Life: "The Committee noted that in an indirect comparison, pazopanib had statistically significantly less fatigue compared with sunitinib". Fatigue is a debilitating side effect that interferes with the patient's ability to work, volunteer and enjoy quality of life. Based upon this difference alone, many patients would want to be able to make a CHOICE without necessarily having to prove intolerant to the fatigue (and other side effects) caused by another treatment first. Fatigue (often resulting from hypothyroidism) is cumulative – i.e., not easily determined by one or two cycles of therapy.
4	Overall Clinical Benefit Safety: Low incidence of hand-foot syndrome	Paragraph 7	On Hand-foot syndrome as a profound detriment to Quality of Life: Patients should not have to be subjected to intolerable blisters on their feet and hands simply to prove qualification for a treatment with a lower incidence of these adverse effects. Informed patients and oncologists need to be able to make the right choice at the right time based upon the patient's individual profile and work/life circumstances.

Additional comments about the initial recommendation document

Please provide any additional comments:

Page Number	Section Title	Paragraph, Line Number	Additional Comments
			Given the 3-page limit on comments from a Patient Advocacy Group, we have no room for further comments.

About Completing This Template

pCODR invites those registered patient advocacy groups that provided input on the drug under review **prior** to deliberation by the pCODR Expert Review Committee (pERC), to also provide feedback and comments on the initial recommendation made by pERC. (See www.pcodr.ca for information regarding review status and feedback deadlines.)

As part of the pCODR review process, the pCODR Expert Review Committee makes an initial recommendation based on its review of the clinical, economic and patient evidence for a drug. (See www.pcodr.ca for a description of the pCODR process.) The initial recommendation is then posted for feedback and comments from various stakeholders. The pCODR Expert Review Committee welcomes comments and feedback that will help the members understand why the patient advocacy groups agree or disagree with the initial recommendation. In addition, the members of pERC would like to know if there is any lack of clarity in the document and if so, what could be done to improve the clarity of the information in the initial recommendation. Other comments are welcome as well.

All stakeholders have 10 (ten) business days within which to provide their feedback on the initial recommendation and rationale. If all invited stakeholders, including registered patient advocacy groups, agree with the recommended clinical population described in the initial recommendation, it will proceed to a final pERC recommendation by 2 (two) business days after the end of the consultation (feedback) period. This is called an "early conversion" of an initial recommendation to a final recommendation.

If any one of the invited stakeholders does not support the initial recommendation proceeding to final pERC recommendation, pERC will review all feedback and comments received at the next possible pERC meeting. Based on the feedback received, pERC will consider revising the recommendation document as appropriate. It should be noted that the initial recommendation and rationale for it may or may not change following consultation with stakeholders.

The final pERC recommendation will be made available to the participating provincial and territorial ministries of health and cancer agencies for their use in guiding their funding decisions and will also be made publicly available once it has been finalized.

Instructions for Providing Feedback

a) Only registered patient advocacy groups that provided input at the beginning of the review of the drug can provide feedback on the initial recommendation.

- Please note that only one submission per patient advocacy group is permitted. This applies to those groups with both national and provincial / territorial offices; only one submission for the entire patient advocacy group will be accepted. If more than one submission is made, only the first submission will be considered.
- Individual patients should contact a patient advocacy group that is representative of their condition to have their input added to that of the group. If there is no patient advocacy group for the particular tumour, patients should contact pCODR for direction at info@pcodr.ca.

b) Feedback or comments must be based on the evidence that was considered by pERC in making the initial recommendation. No new evidence will be considered during this part of the review process; however, it may be eligible for a Resubmission.

c) The template for providing *pCODR Patient Advocacy Group Feedback on a pERC Initial Recommendation* can be downloaded from the pCODR website. (See www.pcodr.ca for a description of the pCODR process and supporting materials and templates.)

d) At this time, the template must be completed in English. Patient advocacy groups should complete those sections of the template where they have substantive comments and should not feel obligated to complete every section, if that section does not apply to their group. Similarly, groups should not feel restricted by the space allotted on the form and can expand the tables in the template as required.

e) Feedback on the initial pERC recommendations should not exceed three (3) pages in length, using a minimum 11 point font on 8 ½″ by 11″ paper. If comments submitted exceed three pages, only the first three pages of feedback will be forwarded to the pERC.

f) Feedback should be presented clearly and succinctly in point form, whenever possible. The issue(s) should be clearly stated and specific reference must be made to the section of the recommendation document under discussion (i.e., page number, section title, and paragraph). Opinions from experts and testimonials should not be provided. Comments should be restricted to the content of the initial recommendation.

g) References to support comments may be provided separately; however, these cannot be new references. New evidence is not considered during this part of the review process, however, it may be eligible for a Resubmission. If you are unclear as to whether the information you are considering to provide is eligible for a Resubmission, please contact the pCODR Secretariat.

h) The comments must be submitted via a Microsoft Word (not PDF) document by logging into www.pcodr.ca and selecting "Submit Feedback" by the posted deadline date.

i) If you have any questions about the feedback process, please e-mail submissions@pcodr.ca. Information about pCODR may be found at www.pcodr.ca. For more information regarding patient input into the pCODR drug review process, see the *pCODR Patient Engagement Guide*. Should you have any questions about completing this form, please email submissions@pcodr.ca

Note: Submitted feedback may be used in documents available to the public. The confidentiality of any submitted information cannot be protected.