PAN-CANADIAN ONCOLOGY DRUG REVIEW

pan-Canadian Oncology Drug Review Submitter or Manufacturer Feedback on a pCODR Expert Review Committee Initial Recommendation

Crizotinib (Xalkori) Advanced NSCLC

October 4, 2012

3 Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s)	**XALKORI (crizotinib)** is indicated as monotherapy for use in patients with anaplastic lymphoma kinase (ALK)-positive advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC).
Role in Review (Submitter and/or Manufacturer):	Submitter and manufacturer
Organization Providing Feedback	Pfizer Canada Inc.

3.1 Comments on the Initial Recommendation

a) Please indicate if the Submitter (or the Manufacturer of the drug under review, if not the Submitter) agrees or disagrees with the initial recommendation:

_____ agrees ___ __ agrees in part __ X ___ disagree

Please explain why the Submitter (or the Manufacturer of the drug under review, if not the Submitter) agrees, agrees in part or disagrees with the initial recommendation.

Pfizer disagrees with the initial negative recommendation as the manufacturer is convinced of the unprecedented extent of benefits Xalkori has to offer to NSCLC patients characterized with ALK positive mutation as signalled through its Phase I/II clinical program. We felt that this was also reflected by the clinical guidance panel where their conclusion is: ... *In the meantime, with establishment of appropriate routine companion ALK mutation testing, the panel felt it is clinically reasonable for ALK-positive advanced/metastatic patients to have access to crizotinib at some point in the course of their disease.*

The main expectation highlighted by pERC to inform their forthcoming final recommendation was to obtain confirmation of the early benefit signals highlighted in our Phase I/II studies 1001 and 1005 through our Phase III data from the 1007 trial.

Despite the confidential nature of this data until its publication at the end of September 2012, Pfizer has developed an internal process to allow privileged sharing of the 1007 results with pCODR to help move towards a favourable recommendation. Pfizer would have welcomed the opportunity to expedite the review and accelerate the process towards patient reimbursement by taking advantage of the initial recommendation time period to engage in sharing with pCODR/pERC the results of the 1007 data.

However, the manufacturer was informed by pCODR that a resubmission is the only option that can accommodate the presentation of the 1007 results. The manufacturer emphasizes that a revision to the pCODR process to accommodate new clinical data as it evolves would better align to the realities of oncology care characterized by significant and rapid evidence generation, dissemination and integration into bedside care. A revision to the current pCODR process would better serve the common goals of more timely decisions impacting patient care.

Given the current process, Pfizer is planning to adapt its submission as rapidly as possible and adopt the resubmission path that will minimize time to final recommendation while meeting pCODR's requirements for a complete submission.

b) Notwithstanding the feedback provided in part a) above, please indicate if the Submitter (or the Manufacturer of the drug under review, if not the Submitter) 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.	_____ Do not support conversion to final recommendation.
Recommendation does not require reconsideration by pERC	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?

Note: no additional comments were submitted to pCODR by Pfizer Canada Inc.

About Completing This Template

pCODR invites the Submitter, or the Manufacturer of the drug under review if they were not the Submitter, to 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 Submitter (or the Manufacturer of the drug under review, if not the Submitter), agrees or disagrees 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 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 the group making the pCODR Submission, or the Manufacturer of the drug under review can provide feedback on the initial recommendation.

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 at this part of the review process, however, it may be eligible for a Resubmission.

c) The template for providing *Submitter or Manufacturer Feedback on 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. The Submitter (or the Manufacturer of the drug under review, if not the Submitter) 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. Similarly, the Submitter (or the Manufacturer of the drug under review, if not the Submitter) 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 pERC Initial Recommendation 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 related to new evidence. New evidence is not considered at 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 to the pCODR Secretariat by the posted deadline date.

i) If you have any questions about the feedback process, please e-mail submissions@pcodr.ca.

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