PAN-CANADIAN ONCOLOGY DRUG REVIEW

pan-Canadian Oncology Drug Review

Provincial Advisory Group (PAG) Feedback on a pCODR Expert Review Committee Initial Recommendation

Afatinib (Giotrif) for Advanced Non-Small Cell Lung Cancer

May 2, 2014

3 Feedback on pERC Initial Recommendation

Name of the drug indication(s): Afatinib (Giotrif) for advanced NSCLC

Endorsed by: Provincial Advisory Group Chair

Feedback was provided by eight of nine provinces (Ministries of Health and/or provincial cancer agencies) participating in pCODR.

3.1 Comments on the Initial Recommendation

a) Please indicate if the PAG (either as individual PAG members and/or as a group) agrees or disagrees with the initial recommendation:

_____ Agrees ___X__ Agrees in part ____ Disagree

PAG members, in general, agree in part with the pERC initial recommendation on afatinib for first-line treatment of NSCLC.

PAG agrees with pERC's assessment of the data on afatinib when compared to cisplatin-pemetrexed and when compared to cisplatin-gemcitabine. PAG noted that the economic data for gemcitabine/cisplatin is lacking and agreed with pERC that a resubmission with this data would be reasonable.

However, PAG noted that the economic analysis comparing afatinib to pemetrexed is based on the pemetrexed list price and that using lower real-world prices of pemetrexed could alter the results of the economic analysis.

PAG disagrees with the recommendation as it relates to other tyrosine kinase inhibitors (TKIs). PAG requested that pERC review the consistency of the recommendation compared with other reviews where the drug was only compared to placebo and where pERC had recommended the drug as an alternative in the same treatment space. PAG members indicate they would prefer a recommendation that allows for physician/patient choice of TKI in provinces/territories that already fund a TKI.

PAG thought that implementing the two separate recommendations would be confusing and would not provide consistency of afatinib funding across Canada. PAG appreciated pERC's attention to the differences in funding of current treatment options across Canada, but would find recommendations that rely primarily on evidence (e.g. clinical, economic) and patient values more useful than recommendations that depend on what each province/territory is currently funding. It was thought this issue could be addressed in a Next Step for provinces, rather than in the recommendation itself.

b) Notwithstanding the feedback provided in part a) above, please indicate if the PAG 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.

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

PAG members do not support conversion to final recommendation and the recommendation should be reconsidered by pERC on the following:

- Although the available data does not allow one to directly compare afatinib to any other TKI, there is belief that afatinib has a PFS advantage over platinum-based chemotherapy. Further, at the time the trial was designed, the TKI therapy was not routinely available, so it is hard to dismiss the results of this trial on the basis that it does not compare afatinib to another TKI. (It is also noted that the level of evidence to support afatinib is the same as gefitinib.) Finally, it is noted that there are multiple drugs of the same family reimbursed without direct comparative data (e.g., aromatase inhibitors).
- Gefitinib would be the most appropriate comparator for afatinib, rather than chemotherapy, in provinces that already fund gefitinib. Although PAG understands that it could be appropriate to wait for the results of the head-to-head trial prior to making a recommendation to fund afatinib as a *replacement* of gefitinib in the treatment of first-line NSCLC, PAG would like pERC to reconsider whether afatinib could be recommended as an *alternate* TKI, using the currently available trial or indirect comparison data, which would provide treatment choices to the physicians/patients.
- PAG prefers one recommendation based on a thorough and comprehensive consideration of the clinical evidence, patient values and economic analysis, rather than separate recommendations depending on what each province/territory is currently funding. The individual provinces can then decide where afatinib would fit into their current treatment algorithm and drug funding.

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?

Page Number	Section Title	Paragraph, Line Number	Comments and Suggested Changes to Improve Clarity
1	pERC Recommendation	Paragraph #1, line #7 and #11	Suggest clarifying the term "replacement therapy". Does it imply a switch in therapy for patients who are treatment naïve and patients who are already on cisplatin-pemetrexed first line therapy?
1	pERC Recommendation	Paragraph #1, Line 11-12	Clarification is needed in that Afatinib is cost-effective in relation to Cisplatin-Pemetrexed only at the list price. The cost-effectiveness

			of Afatinib will be difficult to interpret for provincial jurisdictions in that there are very significant cost reductions of Pemetrexed from list price.
1	pERC Recommendation	Paragraph #2	recommendation is not consistent with other drugs that have been reviewed that do not have direct comparative data with current standard of care, but yet have evidence for benefit.
3	Summary of pERC Deliberations	Paragraph #2, line #10	Suggest elaborating on the term "manageable". Were diarrhea and dermatologic side effects deemed manageable because the low rates of discontinuation and treatment related mortality
4	Evidence in Brief – Overall Clinical Benefit	Paragraph #2, Line #8	Dosing does not align with the LUX-Lung 6 trial, where gemcitabine is given on day 1 and day 8 plus cisplatin 75 mg/m² on day 1 of a 3-week cycle
7	Economic Evaluation	Paragraph #7, Line #2-6	Dosing does not align with the LUX-Lung 6 trial, where gemcitabine is given on day 1 and day 8 plus cisplatin 75 mg/m² on day 1 of a 3-week cycle

3.2 Comments related to PAG input

Please provide feedback on any issues not adequately addressed in the initial recommendation based on the PAG input provided at the outset of the review on potential impacts and feasibility issues of adopting the drug within the health system.

Page Number	Section Title	Paragraph, Line Number	Comments related to initial PAG input
7	Economic Evaluation	Paragraph #5	Only the potential impact of flat pricing and dose reductions was discussed. What about the potential impact of flat pricing and dose escalation?

3.3 Additional comments about the initial recommendation document

Please provide any additional comments:

Page Number	Section Title	Paragraph, Line Number	Additional Comments
	Drug and Condition Information		"current standard treatment"- Tarceva is currently funded as second AND third line treatments in Ontario.
5	Overall Clinical	paragraph 2, line#9	suggest replacing the term "platinum-based" with

	Benefit		"cisplatin-based".
5	Overall Clinical Benefit – Quality of Life		Suggest specifying qualify of life assessments used in the pivotal trials (e.g. self-administered questionnaires, the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire C30 (QLQ-C30) and lung cancer-specific module (QLQ-LC13).
5	Overall Clinical Benefit	paragraph#6, line #6-7	suggest clarifying the term "clinical validity". Does the analysis lack clinical validity because of the limitations of relying on indirect and cross trial comparisons?
6	Overall Clinical Benefit	paragraph #2, line 9-10	Suggest removing line "these agents are now established as standard of care in this patient population." Tarceva is not funded in 1st line setting for all provinces and it is unclear whether it is a standard of care in this patient population in Canada.
6	Overall Clinical Benefit	paragraph #2, line 11-12	Tarceva is currently funded as second AND third line treatments in Ontario

About Completing This Template

pCODR invites the Provincial Advisory Group (PAG) to provide feedback and comments on the initial recommendation made by the pCODR Expert Review Committee. (See www.pcodr.ca for information regarding review status and feedback deadlines.)

As part of the pCODR re view 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 pERC 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 PAG, either as individual PAG members and/or as a group, agrees or disagrees with the pERC 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 pERC 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 pERC final 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 a pERC final 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 pERC final 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 members of the PAG can provide feedback on the pERC initial recommendation; delegates must work through the PAG representative to whom they report.
    a. Please note that only one submission is permitted for the PAG. Thus, the feedback should include both individual PAG members and/or group feedback.

b) Feedback or comments must be based on the evidence that was considered by pERC in making the pERC 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 *Provincial Advisory Group (PAG) 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. PAG 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, PAG 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.