pCODR PAN-CANADIAN ONCOLOGY DRUG REVIEW

pCODR EXPERT REVIEW COMMITTEE (pERC)
FINAL RECOMMENDATION

The pan-Canadian Oncology Drug Review (pCODR) was established by Canada's provincial and territorial Ministries of Health (with the exception of Quebec) to assess cancer drug therapies and make recommendations to guide drug-funding decisions. The pCODR process brings consistency and clarity to the cancer drug assessment process by looking at clinical evidence, cost-effectiveness and patient perspectives.

pERC Final Recommendation
Upon consideration of feedback from eligible stakeholders, pERC members considered that criteria for early conversion of an Initial Recommendation to a Final Recommendation were met and reconsideration by pERC was not required.

Drug: Crizotinib (Xalkori) **Submitted Funding Request:** As monotherapy in patients with anaplastic lymphoma kinase (ALK)-positive locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC)	
Submitted By: Pfizer Canada Inc.	**Manufactured By:** Pfizer Canada Inc.
NOC Date: April 25, 2012	**Submission Date:** February 17, 2015
Initial Recommendation: July 3, 2015	**Final Recommendation:** July 21, 2015

Erratum: This is a revised Final pERC Recommendation which supersedes the Final pERC Recommendation for this drug and indication dated July 21, 2015. The submitter notified pCODR of an erratum in the New England Journal of Medicine for the PROFILE 1014 trial, which was a pivotal trial analyzed in pCODR's review. The erratum is regarding a change in the time to deterioration in patient reported lung cancer symptoms. The erratum does not change the overall conclusions of the Clinical Guidance Panel or pERC's final recommendation.

pERC RECOMMENDATION

The pCODR Expert Review Committee (pERC) recommends funding crizotinib (Xalkori) conditional on the cost-effectiveness of crizotinib being improved to an acceptable level. Funding should be for first-line treatment of patients with ALK-positive non-small cell lung cancer with an ECOG performance status of 0 – 2. Treatment should be continued until disease progression or unacceptable toxicity.

The Committee made this recommendation because it was satisfied that there was a net clinical benefit of crizotinib based upon statistically significant and clinically meaningful improvement in progression-free survival, improvement in time to deterioration of lung cancer symptoms and improvement in quality of life compared to standard chemotherapy. Crizotinib in this population also aligns with patient values. However, the Committee noted that, at the submitted price and best estimates of the incremental cost-effectiveness ratio, crizotinib is not cost-effective compared with standard care.

POTENTIAL NEXT STEPS FOR STAKEHOLDERS	**Pricing Arrangements to Improve Cost-Effectiveness** Given that there is a net clinical benefit of crizotinib, jurisdictions may want to consider pricing arrangements and/or cost structures that would improve the cost-effectiveness of crizotinib to an acceptable level. pERC noted that jurisdictions may also want to consider the impact of dose adjustments on tablet burden since crizotinib is priced per tablet and not per milligram (e.g. a reduction from 250mg to 200mg would not result in a price reduction). **Time-Limited Need for Crizotinib** At the time of implementing a funding recommendation for crizotinib, jurisdictions may consider addressing the short-term, time-limited need for crizotinib for those patients with ALK positive disease who are currently receiving first line chemotherapy or who have recently completed a first-line treatment. pERC noted that this time-limited access should be for patients who otherwise meet the eligibility criteria of the PROFILE 1014 study.

SUMMARY OF pERC DELIBERATIONS

Lung cancer is the leading cause of cancer-related deaths worldwide with the majority of the patients presenting with non-curable disease. ALK mutations occur in approximately 4% of non-small cell lung cancers, representing about 400-500 patients annually in Canada. For patients with advanced non-small cell lung cancer (NSCLC), including those with ALK-mutation positive disease, standard treatments in the first-line setting include intravenous chemotherapy with platinum-based doublet therapy. Pemetrexed plus platinum chemotherapy is the standard first line treatment for non-squamous lung cancer, which is the most common form of NSCLC in Canada. While chemotherapies used in the treatment of NSCLC are associated with improvements in overall survival and quality of life, these improvements are modest and most patients with metastatic disease experience disease progression with a median time to progression of approximately four months. pERC agreed there is a need for more effective therapeutic options with manageable toxicity in this patient population.

pERC's Deliberative Framework for drug funding recommendations focuses on four main criteria:	
CLINICAL BENEFIT	**PATIENT-BASED VALUES**
ECONOMIC EVALUATION	**ADOPTION FEASIBILITY**

pERC deliberated upon the results of one randomized controlled trial, PROFILE 1014(Solomon et al 2014),which compared crizotinib to pemetrexed-plus-platinum chemotherapy in previously-untreated patients with ALK-positive, advanced or metastatic NSCLC. Based on a clinically meaningful and statistically significant improvement in progression-free survival (PFS), statistically significant improvement in time to deterioration of lung cancer symptoms and in quality of life, pERC considered that there was a net clinical benefit associated with crizotinib in previously untreated patients. pERC noted that the separation of the Kaplan Meier curves for PFS beyond the median was impressive; this and the hazard ratio indicate that crizotinib provides a meaningful PFS benefit for patients. pERC also discussed that a large proportion of patients switched over from the chemotherapy arm to the crizotinib arm (67.3%) and agreed that this may have resulted in confounding of the survival benefit from crizotinib, which means that measuring a significant improvement in overall survival may be difficult. Additionally, the Committee noted that the medians for overall survival had not been reached in either arm at the end of the trial period and acknowledged that the unusually high proportion of patients alive in both arms at36 months suggested a possible survival benefit with crizotinib. Finally, pERC discussed safety data from PROFILE 1014 and noted that crizotinib appeared to be generally well-tolerated by patients, with an acceptable toxicity profile. The majority of adverse events were grades 1 and 2.Grade 3 and 4 adverse events were also similar between the two arms.

pERC deliberated upon input from patient advocacy groups concerning crizotinib and noted that prolonging PFS and improving quality of life were important to patients. Access to an oral therapy was also an expressed patient value. The PROFILE 1014study demonstrated a clinically and statistically significant improvement in PFS, improvement in deterioration of lung cancer symptoms and improvements in quality of life for patients receiving crizotinib compared with standard of care. pERC also noted that patients providing input and who have experience with crizotinib reported a rapid improvement in symptoms. As crizotinib is an oral treatment, pERC agreed that treatment would likely be much easier for patients to take and would not require as much personal and caregiver time and resources (e.g., trips to the hospital) compared with intravenous chemotherapies. Therefore, pERC considered that crizotinib clearly aligns with patient values.

pERC deliberated upon the cost-effectiveness of crizotinib and concluded that it is not cost effective. pERC considered estimates provided by the submitter and reanalysis conducted by the pCODR Economic Guidance Pane(EGP) and agreed with the EGP that uncertainty around the time horizon and probability of post progression survival and mortality included in the submitted economic model had the largest impact on the incremental cost effectiveness ratio. While pERC acknowledged that there may be OS benefit with crizotinib, there remains uncertainty around the magnitude of any long term survival benefit with crizotinib. Therefore the Committee supported the use of a more conservative approach and agreed with the EGP in shortening the time horizon within the model to align with the trial data. The committee also agreed that extrapolation beyond progression and the trial period for estimates of survival is challenging

because the probability of survival is influenced by subsequent therapies. Based on these discussions, pERC accepted the range of cost-effectiveness estimates provided by the EGP and agreed that crizotinib is not cost-effective, concluding that the true ICER is likely in the middle of the range of the EGP`s estimate.

pERC also considered factors affecting the feasibility of implementing a positive funding recommendation for crizotinib in the first line setting. pERC noted that ALK testing is now widely available in the second line setting. While acknowledging the budgetary impact of ALK testing, pERC noted that ALK testing is already widely available and, therefore, access for testing in the first line setting should not be a barrier, though ALK testing will now be required earlier in their disease trajectory. pERC, therefore, concluded that ALK testing in the first line setting will not have a significant impact on incremental budget impact of testing overall. pERC also discussed treatment sequencing and agreed with the Clinical Guidance Panel that, for eligible patients, crizotinib is a preferable treatment in the first line setting as declining performance status post chemotherapy may make patients ineligible for crizotinib in the second line setting. pERC was, however, unable to comment on sequencing of other treatments after progression on crizotinib as there was no data available to determine optimal sequencing of subsequent therapies.

CONTEXT OF THE RESUBMISSION

A submission and resubmission for crizotinib (Xalkori) for patients with anaplastic lymphoma kinase-(ALK) positive advanced non-small cell lung cancer (NSCLC) were previously received by pCODR. The first submission on March 26, 2012 with the pERC Final Recommendation issued on October 4, 2012 and the first resubmission received on October 23, 2012 with the pERC Final Recommendation issued on May 2, 2013.

- The pERC Final Recommendation on the first submission was to not recommend funding crizotinib (Xalkori) for patients with ALK-positive advanced non-small cell lung cancer. The Committee made this recommendation because they were not confident of the net clinical benefit of crizotinib due to limitations in the evidence available from clinical trials at the time.
- The pERC Final Recommendation on the first resubmission was to recommend funding crizotinib as a second-line therapy for patients with ALK-positive advanced NSCLC with ECOG performance status ≤ 2, conditional on the cost-effectiveness of crizotinib being improved to an acceptable level.
- At the time, the Committee noted that there was one ongoing randomized controlled trial in untreated patients evaluating crizotinib compared with pemetrexed plus a platinum agent, PROFILE 1014.
    - As pre-specified criteria (i.e. stopping rules) had not been met that would provide sufficient reason to stop PROFILE 1014 early and accept crizotinib as the standard first-line treatment for all patients in the trial, pERC had agreed it was ethical to wait for the results of this trial to inform any potential use in first line patients.
    - pERC also noted that patients were awaiting results of the trial in the first-line setting.
- This second resubmission was made by the manufacturer and provided new clinical and economic information on the use of crizotinib in the first line setting and is supported by the results of PROFILE 1014. Therefore the current review focused only on the use of crizotinib in first line setting.

EVIDENCE IN BRIEF

pERC deliberated upon:

- a pCODR systematic review
- other literature in the Clinical Guidance Report providing clinical context
- an evaluation of the manufacturer's economic model and budget impact analysis
- guidance from pCODR clinical and economic review panels
- input from two patient advocacy groups (Lung Cancer Canada & Ontario Lung Association)
- input from pCODR's Provincial Advisory Group.

Feedback on the pERC Initial Recommendation was also provided by:

- input from pCODR's Provincial Advisory Group.
- the Submitter (Pfizer Canada Inc.)

The pERC initial recommendation was to fund crizotinib (Xalkori) conditional on the cost-effectiveness of crizotinib being improved to an acceptable level. Funding should be for first-line treatment of patients with ALK-positive non-small cell lung cancer with an ECOG performance status of 0 – 2. Treatment should be continued until disease progression or unacceptable toxicity. Feedback on the pERC Initial Recommendation indicated that the manufacturer and the pCODR's Provincial Advisory Group agreed with the Initial Recommendation.

The pERC Chair and pERC members reviewed the feedback and it was determined that the pERC Initial Recommendation was eligible for early conversion to a pERC Final Recommendation without reconsideration by pERC because there was unanimous consensus from stakeholders on the recommended clinical population outlined in the pERC Initial Recommendation.

OVERALL CLINICAL BENEFIT

pCODR review scope

The purpose of the review was to evaluate the effect of crizotinib (Xalkori) on patient outcomes compared with standard therapies or placebo in previously untreated patients with anaplastic lymphoma kinase (ALK) positive or metastatic non-small cell lung cancer (NSCLC).

Studies included: One RCT in previously untreated patients

The pCODR systematic review included one open-label phase III trial, PROFILE 1014, which randomized previously untreated patients with ALK-positive, advanced or metastatic NSCLC 1:1 to receive crizotinib (n=172) or pemetrexed-plus-platinum chemotherapy (n=171). The choice of platinum chemotherapy (carboplatin or cisplatin) was made by the investigator.

The pCODR review also provided contextual information on ALK mutation testing. pERC noted that ALK testing is now widely available in the second line setting. Therefore, the availability of crizotinib in an earlier line of therapy would only require that patients be tested earlier in their disease trajectory, although the number of patients tested could potentially be greater.

Patient populations: Most patients with ECOG performance status 0 or 1

The demographic and baseline characteristics for patients in PROFILE 1014 were well balanced between the crizotinib and pemetrexed-plus-platinum chemotherapy groups, which means the randomization method used in the trial was effective. Patients had a median age of 52-54 years and over 60% were female. The majority of patients had an ECOG PS of 0-1(94% and 95%, respectively in the crizotinib and chemotherapy arms), however a small number of patients with ECOG PS of 2 were included also. In addition, most of the patients were either never-smokers or former smokers, had a histological subtype of adenocarcinoma and had no brain metastases. Among the 171 patients randomized to the pemetrexed-plus-platinum chemotherapy arm, 53.2% vs. 45.6% of patients received cisplatin vs. carboplatin, respectively as the combination therapy with pemetrexed. Early treatment switching (ie. crossover) was allowed in the study and 109 patients (63.7%) in the pemetrexed-plus-platinum chemotherapy group switched to the crizotinib group upon disease progression. pERC discussed the large proportion of patients that switched into the crizotinib arm and agreed that the overall survival results were likely confounded.

Key efficacy results: Clinically meaningful improvement in PFS

The key efficacy outcome deliberated on by pERC was progression-free survival (PFS). Crizotinib significantly prolonged PFS with a median PFS of 10.9 months compared to 7.0 months for patients in the pemetrexed-plus-platinum chemotherapy group[hazard ratio (HR) 0.45 95% CI: 0.35-0.60]. pERC considered that this improvement in PFS was both statistically significant and clinically meaningful. pERC also discussed results from a pre-specified interim overall survival analysis which did not show a statistically significant difference between arms and agreed this was likely confounded by the substantial proportion of patients switching into the crizotinib arm. pERC however acknowledged that the unusually high proportion of patients alive in both arms at 36 months suggested a possible survival benefit with crizotinib. Objective response rate was also significantly higher with crizotinib than with chemotherapy (74.4% vs. 45.0%, $p<0.001$).

Quality of life: Improvements in time to deterioration of lung cancer symptoms and QoL scales

PROFILE 1014 demonstrated a statistically significant improvement from baseline in global quality of life in patients with crizotinib vs. pemetrexed-plus-platinum chemotherapy. This was also observed in physical, social, emotional, and role functioning domains. A statistically significant reduction from baseline in a number of symptoms on the QLQ-C30 and QLQ-LC13 scales was also observed with crizotinib. A statistically significant improvement was also measured in the time to deterioration of lung cancer symptoms (HR 0.59 95% CI 0.45-0.77, p<0.001). pERC agreed that these improvements in quality of life and in disease and drug related symptoms were of high importance to patients.pERC considered whether the minimally clinically important differences of 10 points was observed in any of these measures and noted that some of the measures demonstrated a difference of 10 point or more from baseline. However, most of the quality of life scales did not demonstrate a minimal clinically important difference.

Safety: Acceptable toxicity profile

pERC deliberated upon the adverse events observed in PROFILE 1014 and noted that crizotinib has a safety profile that is comparable with other oral targeted anticancer therapies used in NSCLC management. The majority of events in both treatment groups were grade 1 or 2 in severity and adverse events leading to discontinuation were low in frequency. pERC discussed that serious adverse events occurred in a similar proportion of patients, 33.9% and 27.8% of patients receiving crizotinib and pemetrexed-plus-platinum chemotherapy, respectively. Grade 3 to 4 adverse events were similar between the crizotinib and chemotherapy groups, except for elevated transaminases occurring in 14.0% vs. 2.4% of patients receiving crizotinib compared with chemotherapy, respectively. pERC however, noted that elevated transaminases, while clinically relevant, do not significantly reduce patients' quality of life. The results of the study were also in alignment with input, provided by patients, who expressed the view that most of the side effects experienced with crizotinib were minimal and manageable in nature.

Need: effective and tolerable treatment options

For patients with advanced non-small cell lung cancer (NSCLC), including those with ALK-mutation positive disease, standard treatment in the first-line setting consists of intravenous chemotherapy with a platinum-based doublet therapy, such as cisplatin or carboplatin combined with one of gemcitabine, vinorelbine, paclitaxel, docetaxel, or pemetrexed. pERC noted that while the chemotherapies used in the treatment of NSCLC are associated with improvements in overall survival and quality of life, these improvements are modest and most patients with metastatic disease experience disease progression with a median time to progression of approximately four months. Although the ALK-positive population represents a small proportion of all advanced or metastatic NSCLC in Canada, the annual incidence of NSCLC is large thus yielding a modest number of ALK-positive patients in need of more effective and tolerable treatment option in the first line setting.

PATIENT-BASED VALUES

Values of patients with advanced NSCLC: Highly symptomatic with a substantial impact on daily living

Patient advocacy group input indicated that lung cancer has a tremendous negative impact on the daily lives of patients and is a devastating illness. Symptoms most frequently experienced by patients include fatigue, loss of appetite, shortness of breath, cough, pain, and blood in sputum. Loss of appetite, cough, pain, and shortness of breath were found to be significant quality of life predictors. Lung cancer was also reported to impact many aspects of day-to-day life for patients living with the disease including ability to work, travel, socialize and participate in leisure and physical activities. In addition, patient's relationships with loved ones, emotional well-being and financial circumstances also suffer. Furthermore, pERC noted that patients with lung cancer are often burdened with the stigma associated with smoking as the leading cause of their cancer, although ALK-positive NSCLC more often occurs in never-smokers. pERC, therefore, agreed that improvements in symptom control and quality of life were important to patients and that a statistically significant improvement in time to deterioration of symptoms and quality of life was observed in PROFILE 1014, which aligns with patient values.

Patient values on treatment: Improvements in PFS, fast symptom management and QoL

pERC noted that most patients with NSCLC receive chemotherapy for first-line treatment of NSCLC. Some patients, however, are deemed unsuitable for chemotherapy for reasons of performance status, age or

other illnesses. For those that receive chemotherapy, treatment is associated with severe side effects including nausea, vomiting, hair loss, fatigue and the risk of fever and infection. Patients therefore consider an improvement in efficacy, convenience or side effect profile over current therapies to be important aspects for consideration. Patients also noted an appreciation for minimal to no cost burden associated with new treatments, as well as at-home administration. pERC agreed that the statistically significant and clinically meaningful improvements in median PFS and statistically significant improvements in QoL observed in PROFILE 1014 aligned with the patients expressed values.

pERC also noted the tremendous burden on patients and their caregivers, who must take time off from work to receive treatment, and then additional time off to manage chemotherapy toxicity, including frequent admission to hospital. The cost of travel was highlighted as an additional burden, more so in rural communities where there is a desire for fewer medical appointments, as well as a wish for a lower cost burden on patients. pERC noted that crizotinib is an oral therapy, which would improve convenience of treatment for patients with ALK-positive advanced NSCLC. Oral treatments may be easier for patients to take and would not require as much personal and caregiver time and resources (e.g., trips to the hospital) as would be required for intravenous chemotherapies. However, pERC also noted that some patients may have difficulty accessing crizotinib as access to oral therapies varies across the country.

pERC noted that 9patients were identified who had experience with crizotinib, of whom4 were receiving crizotinib for first-line treatment. Many of these patients were reported to be active and high functioning, and living longer than 2 years on treatment. Mild nausea and diarrhea were the most commonly reported side effects seen in more than one quarter of patients. Generally, side effects were reported as being manageable for patients and, most importantly, crizotinib was reported to have dramatically improved outcomes. pERC agreed that the experience of patients on crizotinib aligned with the results of PROFILE 1014. Patients described crizotinib as having helped them return to normal life, to continue to work and to parent their children. For patients with symptoms, crizotinib was felt to work quickly, while having manageable side effects.

ECONOMIC EVALUATION

Economic model submitted: Cost-effectiveness and cost-utility

The pCODR Economic Guidance Panel assessed an economic evaluation of the cost-effectiveness and cost-utility of crizotinib compared with the current standard of care for patients with locally advanced or metastatic ALK-positive Non-Small Cell Lung Cancer (NSCLC).

Basis of the economic model: Clinical and economic inputs

Costs included drug treatment acquisition cost, molecular diagnostic testing cost as well as costs associated with drug administration and monitoring, management of adverse events and palliative care.

The key clinical outcomes considered in the model provided by the submitter were overall survival, progression-free survival and utilities.

Drug costs: flat pricing, dose adjustments may lead to higher drug costs and wastage

At the list price, crizotinib costs $146.67 per 200 or250 mg tablet; at the recommended dose of 250 mg twice daily, the average cost per day of crizotinib is $293.33 and the average cost per 28-day course is $8,213.34. pERC also noted that crizotinib is priced per tablet and not per milligram, which is a potential barrier to implementation because actual use in clinical practice could increase costs significantly.In scenarios where dose escalations or dose reductions are required, multiple tablets would be necessary, leading to substantial increases in drug costs and potential for wastage of previously dispensed tablets.

At the list price, pemetrexed cost $4.2900per mg. At the recommended dose of 500mg/m^2 on day 1 of every 21 day cycle, pemetrexed costs $173.64per day and $4,862.00 per 28-day course. At the list price, cisplatin cost $5.8594 per mg. At the recommended dose of 75 mg/m^2 IV day 1 every 21 days, cisplatin costs $35.57 per day and $996.10per 28-day course. At the list price, carboplatin cost $0.10per mg. At the recommended dose of AUC 5 IV on day 1 every 21 days, carboplatin costs $2.38 per day and $66.67per 28-day course.

Cost-effectiveness estimates: time horizon and post progression probability of mortality
pERC deliberated upon the cost-effectiveness of crizotinib in the first-line setting and agreed with the EGP's re-analysis estimates. pERC noted that the inputs that had the largest impact on the incremental cost-effectiveness ratio included the time horizon of the model and the post progression probability of survival. In considering these inputs, pERC noted that the submitted model assumed survival benefits extended beyond the clinical trial duration and median follow-up periods. pERC discussed the Clinical Guidance Panel's conclusion regarding the uncertainty around the long term survival benefit with crizotinib and the unlikelihood of benefit with crizotinib extending beyond the three years observed in the trial. In light of these considerations, pERC agreed with the conservative approach taken by the EGP in shortening the time horizon to 4 years to better align with the clinical trial data. pERC also discussed the assumptions around the probability of post progression mortality remaining the same, irrespective of subsequent therapies, as modeled in the submitted estimates. pERC agreed that it is not clinically plausible to expect patients to maintain similar probabilities of mortality as they move between different treatments following progression on crizotinib. pERC, therefore, agreed with the Clinical Guidance Panel that patients` probabilities of mortality will be different depending on the treatment they receive following progression, and accepted the EGP's reanalysis estimates adjusting for these factors and concluding that crizotinib is not cost-effective for this indication.

ADOPTION FEASIBILITY

Considerations for implementation and budget impact: flat pricing
pERC considered factors affecting the feasibility of implementing a positive funding recommendation for crizotinib. pERC noted that the use of crizotinib in the first line setting would be within a context where ALK testing is already widely available, only now requiring that patients be tested earlier in their treatment setting. pERC therefore agreed that ALK testing in the first line setting will not make a significant difference on the incremental budget impact of testing.

pERC considered that the small patient numbers, oral route of administration and small incremental shift in use of crizotinib from second to first line use are enablers to implementation. pERC discussed the shift of crizotinib from the second to first line and the impact on treatment sequencing. pERC agreed with the Clinical Guidance Panel that crizotinib is a preferable treatment to platinum-based chemotherapy in the first line setting as patients may not be eligible for crizotinib in the second line setting due to disease progression and declining performance status. pERC was however unable to comment on sequencing of other treatment in this context as there was no data available to determine optimal sequencing of subsequent therapies. pERC discussed potential concerns around ocular toxicities and noted that they are not expected to have much impact on additional health care services, as ocular toxicities though common are, typically not severe, and reversible with discontinuation of crizotinib.

pERC also discussed potential barriers to implementation which included the flat pricing of crizotinib tablets and the need for a new prescription upon dose reduction. pERC agreed thatdose escalations or dose reductions that require multiple tablets being dispensed may lead to a substantial increase in drug costs and potential for wastage of previously dispensed tablets.

DRUG AND CONDITION INFORMATION

Drug Information	• Oral anaplastic lymphoma kinase (ALK) selective inhibitor with anti-c-Met and ROS activity • 200 mg and 250 mg tablets • The recommended dose is 250 mg administered orally twice daily • Validated diagnostic test for determining ALK-mutation status required
Cancer Treated	• ALK-positive advanced NSCLC
Burden of Illness	• NSCLC is the leading cause of cancer-related mortality in Canadians • Overall 5-year survival rate of patients with NSCLC is only 17% • There are approximately 400 to 500 ALK positive cases occurring each year in Canada • ALK-gene mutations occur in approximately 4% of lung cancers
Current Standard Treatment	• The current standard of care in Canada for advanced or metastatic NSCLSC in the 1st line setting consists of platinum doublet with either pemetrexed or gemcitabine administered intravenously. • This is followed by crizotinib administered orally as 2nd line • Docetaxel is administered in the 3rd line setting.
Limitations of Current Therapy	• Response rates to chemotherapy are approximately 20% but responses last only a few months, with progression occurring within three to four months and patients requiring alternative treatments options in both the first-line and second-line settings.

ABOUT THIS RECOMMENDATION

The pCODR Expert Review Committee (pERC)
Recommendations are made by the pCODR Expert Review Committee following the pERC Deliberative Framework. pERC members and their roles are as follows:

Dr. Anthony Fields, Oncologist (Chair)
Dr. Maureen Trudeau, Oncologist (Vice-Chair)
Dr. Scott Berry, Oncologist
Bryson Brown, Patient Member
Dr. Matthew Cheung, Oncologist
Mario de Lemos, Pharmacist
Dr. Sunil Desai, Oncologist
Mike Doyle, Economist
Dr. Bill Evans, Oncologist
Dr. Allan Grill, Family Physician
Dr. Paul Hoskins, Oncologist
Danica Wasney, Pharmacist
Carole McMahon, Patient Member Alternate
Jo Nanson, Patient Member
Dr. Tallal Younis, Oncologist
Dr. Kelvin Chan, Oncologist

All members participated in deliberations and voting on the initial recommendation except:

- Dr. Sunil Desai who was not present for the meeting
- Jo Nanson who was the designated non-voting Patient Alternative for this meeting

Because the pERC Initial Recommendation met the criteria for early conversion to a pERC Final Recommendation, reconsideration by pERC was not required and deliberations and voting on the pERC Final Recommendation did not occur.

Avoidance of conflicts of interest

All members of the pCODR Expert Review Committee must comply with the *pCODR Conflict of Interest Guidelines*; individual conflict of interest statements for each member are posted on the pCODR website and pERC members have an obligation to disclose conflicts on an ongoing basis. For the review of the crizotinib (Xalkori) resubmission for first line advanced non-small cell lung cancer, through their declarations, five members had a real, potential or perceived conflict and based on application of the *pCODR Conflict of Interest Guidelines*, none of these members was excluded from voting.

Information sources used

The pCODR Expert Review Committee is provided with a *pCODR Clinical Guidance Report* and a *pCODR Economic Guidance Report*, which include a summary of patient advocacy group and Provincial Advisory Group input, as well as original patient advocacy group input submissions to inform their deliberations. pCODR guidance reports are developed following the pCODR review process and are posted on the pCODR website. Please refer to the pCODR guidance reports for more detail on their content.

Consulting publicly disclosed information

pCODR considers it essential that pERC recommendations be based on information that may be publicly disclosed. All information provided to the pCODR Expert Review Committee for its deliberations was handled in accordance with the *pCODR Disclosure of Information Guidelines*. There was no non-disclosable information in this recommendation document.

Use of this recommendation

This recommendation from the pCODR Expert Review Committee (pERC) is not intended as a substitute for professional advice, but rather to help Canadian health systems leaders and policymakers make well-informed decisions and improve the quality of health care services. While patients and others may use this Recommendation, it is for informational and educational purposes only, and should not be used as a substitute for the application of clinical judgment respecting the care of a particular patient, for professional judgment in any decision-making process, or for professional medical advice.

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