Clinician Input Template for CADTH pCODR Program

***Before completing this template, be sure to*** [***register***](https://drugreviewsadmin.cadth.ca/Landing/Register/Register.aspx?Lang=EN) ***with the pCODR program. Please visit*** [***https://www.cadth.ca/pcodr/registration***](https://www.cadth.ca/pcodr/registration) ***for information about the registration process.***

1. **About the Registered Clinician**

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| Name of Registered Clinician |  |
| Title |  |
| Disease Specialty (if applicable) |  |
| Province |  |
| Organization Membership (if applicable, national or provincial) |  |
| Email |  |
| Telephone Number |  |

If this is a joint clinician input, please list the names of the other clinicians and disease site specialty (if applicable). Please note all clinicians listed must also register with CADTH and complete COI Declarations form.

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Confirmation of Authorship

I declare that I am the author of this submission and to confirm that no other parties have written or participated in the writing of the submission, except for those named above in this joint submission (if applicable).

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| Signature | Date (YYYY/MM/DD) |

1. **About the Drug and Indication Under Review**

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| CADTH pCODR Project Number | pCODR 10206 |
| Generic drug name (Brand name) | Entrectinib (TBD) |
| Indication | ROS1-positive NSCLC |
| Funding Request | As monotherapy for the first-line treatment of patients with ROS1-positive locally advanced or metastatic NSCLC |
| Trial(s) being submitted to pCODR\* | ALKA-372-001 and STARTRK-1 ([NCT02097810](https://clinicaltrials.gov/ct2/show/NCT02097810)) [Drilon, et al. Cancer Discov 2017](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5380583/), [Doebele, et al. WCLC 2018 (Abs. OA02.01)](https://www.roche.com/dam/jcr:3f940849-6f73-4151-8108-f14254040c5e/en/WCLC_Entrectinib_ROS1.pdf" \t "_blank) |
| Health Canada status | Pending |
| U.S. Food & Drug Administration | [August 15, 2019](https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-entrectinib-ntrk-solid-tumors-and-ros-1-nsclc)  Adults with metastatic non-small cell lung cancer (NSCLC) whose tumors are ROS1-positive |
| EMA status | Pending |
| Practice Guidelines\* | [NCCN](https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf) |
| Provincial Funding of Current Treatments or Funding Algorithm | No standard specifically for ROS-1. Standard of care for patients with locally advanced or metastatic NSCLC is chemotherapy (e.g., cisplatin plus pemetrexed). Patients could also receive an ALK inhibitor (e.g., crizotinib) or pembrolizumab. |

\*Please note that access to some online publications require subscription.

1. **Key Questions for Clinician Input**

## 3.1 Current Treatment(s) for the indication under review

* If different than what is listed in the Provincial Funding of Current Treatments in previous page, identify the treatment(s) you would use
* If more than one treatment funded in your province, identify the treatment(s) that would be the most appropriate comparator for the drug under review

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## 3.2 Eligible Patient Population

Describe the patients whom you would use the new treatment. Examples can include, but not limited to, the following questions:

* Does the patient population in the funding request meet the needs in clinical practice? Is there an unmet need?
* Can the inclusion and exclusion criteria of the clinical trial be applied in clinical practice?
* Is there a subgroup of patients beyond the study population that you would like to use the new treatment in? Is there a subgroup of patients within the study population that the new treatment should be limited to?

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**IMPLEMENTATION QUESTIONS**

* + - Can patients have both ROS-1 and NTRK mutations?

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* + - Can patients with ROS-1 mutations be given first-line pembrolizumab if the tumour expresses high PD-L1?

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## Relevance to Clinical Practice

Do you have experience with using the treatment (through clinical trials, manufacturer’s access program, private drug insurance) under review? Yes No

* How or when would you use the new treatment? Is there any population/sub-population where you particularly want to use this drug?
* How is the new treatment different than currently available treatments with respect to efficacy, safety and tolerability?
* Are there contraindications to using the new treatment? Are there contraindications to current treatments that would make the new treatment favorable?

Important Note: Scientific published references are not required, as pCODR has access to current scientific literature through the manufacturer’s submission and a rigorous, independent literature search.

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## 3.4 Sequencing and Priority of Treatments

* Is there evidence to support the optimal sequencing of entrectinib with chemotherapy, crizotinib, and PD-1 or PD-L1 inhibitors (e.g., nivolumab, pembrolizumab, atezolizumab) for ROS-1 NSCLC?

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* In what clinical scenarios (e.g., CNS involvement) would entrectinib or crizotinib be the preferred treatment for ROS-1 NSCLC?

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* Is there evidence to inform use of entrectinib in patients with ROS-1 positive NSCLC who experience CNS disease progression on crizotinib? Would entrectinib be used after crizotinib or other ROS1 targeted agents but before subsequent therapies? Or would entrectinib be used more in later lines or last resort therapy?

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* Is there any evidence to support the use of PD-1 or PD-L1 inhibitors after entrectinib?

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## 3.5 Companion Diagnostic Testing

* If companion diagnostic testing is required for the new drug, is the test available in your jurisdiction? Is it funded by your jurisdiction? What concerns, if any, do you have on the test and turn-around time for test results? Are there specific considerations to a testing algorithm that you think would be important to share with the pCODR Expert Review Committee?

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1. Implementation Questions

Provincial cancer programs across Canada are concerned about the sustainability of high-quality cancer control services. The rising cost of cancer drugs is becoming a major challenge to the sustainability of cancer care funding. While tremendous progress has been made in recent years in how cancer drugs are selected and priced, more needs to be done to ensure innovative treatments are available to patients while ensuring value for money for the public.

Provincial cancer programs are seeking your clinical opinion on the following implementation issues, if and when the new treatment is reimbursed. Your responses would be taken into consideration, amongst other factors, when provincial cancer programs make their final funding decisions.

**4.1 Treatment switching**

* Can patients who started chemotherapy while waiting for ROS-1 test results be switched to entrectinib should the results be positive?

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Appendix A: pCODR Clinician Conflict of Interest Declarations

**Please Note: Each registered clinician must complete their own separate pCODR Clinician Conflict of Interest Declarations Template even if the submission is made jointly.**

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| **Name of registered clinician:** |  |
| **Name of drug and indication under review:** |  |

**Conflict of Interest Declarations**

To maintain the objectivity and credibility of the pCODR process, all participants in the pCODR review process must disclose any conflicts of interest. A registered clinician must declare any potential conflicts of interest that may influence or have the appearance of influencing the information submitted. Conflict of interest declaration is requested for transparency — it does not negate or preclude the use of the clinician input.

Examples of conflicts of interest include, but are not limited to:

* financial support from the pharmaceutical industry or other entities e.g., educational or research grants, honoraria, gifts, and salary;
* affiliations or personal or commercial relationships with drug manufacturers or other interest groups.

***Section A: Payment Received***

1. Have you received any payments over the previous two years from any company or organization that may have direct or indirect interest in the drug under review?

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|  | Yes |
|  | No |

If no, please go to Section B

1. What form of payment did you receive? (Check all that apply.)

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|  | Advisory role (e.g., advisory boards, HTA submission advice) |  | Program or Operating Funding (e.g., website) |  |
|  | Conference attendance |  | Research/educational grants |  |
|  | Royalties |  | Travel grants |  |
|  | Gifts |  | Sponsorship of Events |  |
|  | Honoraria |  | Other, please specify: | \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |

1. Please provide the names of companies and organizations and the amounts of the payments in the box below.

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***Section B: Holdings or Other Interests***

Have you received or is it in possession of stocks or options of more than $10,000 (excluding mutual funds) for organizations that may have a direct or indirect interest in the drug under review? If yes, please list in the table below.

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***Section C: Affiliations, personal or commercial relationships***

Do you have personal or commercial relationships either with a drug or health technology manufacturer (including such manufacturer’s parent corporation, subsidiaries, affiliates and associated corporations) or other interest groups? If yes, please provide the names of the companies and organizations and outline the nature of these relationships in the table below.

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I hereby certify that I have disclosed all relevant information with respect to any matter involving a Party that may place me in a real, potential or perceived conflict of interest situation.

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| --- | --- | --- |
| Date: \_\_\_\_\_\_\_\_\_\_\_\_ | Name: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | Signature:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |